ANTISENSE MODULATION OF FARNESOID X RECEPTOR EXPRESSION

The present application claims priority under Title 35, United States Code, §119 to United States Provisional application Serial No. 60/413,588, filed September 25, 2002, which is incorporated by reference in its entirety as if written herein.

FIELD OF THE INVENTION

[001] The present invention provides compositions and methods for modulating the expression of Farnesoid X Receptor (FXR) alternatively referred to as FXR, RIP14, NR1H4, and Bile Acid Receptor (BAR). In particular, this invention relates to antisense compounds, particularly oligonucleotides, specifically hybridizable with nucleic acids encoding FXR. Such oligonucleotides have been shown to modulate the expression of FXR.

BACKGROUND OF THE INVENTION

[002] Cholesterol is essential for a number of cellular processes, including membrane biogenesis and steroid hormone and bile acid biosynthesis. It is the building block for each of the major classes of lipoproteins found in cells of the human body. Accordingly, cholesterol biosynthesis and catabolism are highly regulated and coordinated processes. A number of diseases and/or disorders have been linked to alterations in cholesterol metabolism or catabolism including atherosclerosis, gallstone formation, and ischemic heart disease. An understanding of the pathways involved in cholesterol homeostasis is essential to the development of useful therapeutics for treatment of these diseases and disorders.

[003] The metabolism of cholesterol to bile acids represents a major pathway for cholesterol elimination from the body, accounting for approximately half of the daily excretion. These cholesterol metabolites are

formed in the liver and secreted into the duodenum of the intestine, where they have important roles in the solubilization and absorption of dietary lipids and vitamins. Most bile acids (approximately 95%) are subsequently reabsorbed in the ileum and returned to the liver via the enterohepatic circulatory system.

[004] Cytochrome P450 7A (CYP7A) is a liver specific enzyme that catalyzes the first and rate-limiting step in one of the two pathways for bile acid biosynthesis (Chiang, J.Y.L. 1998 *Front. Biosci.* **3**:176-193; Russell, D.W. and K.D. Setchell. 1992 *Biochemistry* **31**:4737-4749). The gene encoding CYP7A is regulated by a variety of endogenous, small, lipophilic molecules including steroid and thyroid hormones, cholesterol, and bile acids. Notably, CYP7A expression is stimulated by cholesterol feeding and repressed by bile acids. Thus, CYP7A expression is both positively (stimulated or induced) and negatively (inhibited or repressed) regulated.

[005] CYP7A expression is regulated by several members of the nuclear receptor family of ligand-activated transcription factors (Chiang, J.Y.L. 1998 *Front. Biosci.* **3**:176-193; Gustafsson, J.A. 1999 *Science* **284**:1285-1286; Russell, D.W. 1999 *Cell* **97**:539-542). Recently, two nuclear receptors, the liver X receptor (LXR; NRlH3; Apfel, R. et al. 1994 *Mol. Cell. Biol.* **14**:7025-7035; Willy, P.J. et al. 1995 *Genes Devel.* **9**:1033-1045) and the farnesoid X receptor (FXR; NR1H4; Forman, B.M. et al. 1995 *Cell* **81**:687-693; Seol, W. et al. 1995 *Mol. Endocrinol.* **9**:72-85) were implicated in the positive and negative regulation of CYP7A (Peet, D.J. et al. 1998 *Curr. Opin. Genet. Develop.* **8**:571-575; Russell, D.W. 1999 *Cell* **97**:539- 542). Both LXR and FXR are abundantly expressed in the liver and bind to their cognate hormone response elements as heterodimers with the 9-cis retinoic acid receptor, RXR (Mangelsdorf, D.J. and R.M. Evans. 1995 *Cell* **83**:841-850).

[006] LXR is activated by the cholesterol derivative 24,25(S) epoxycholesterol and binds to a response element in the CYP7A promoter (Lehmann, J.M. et al. 1997 *J. Biol. Chem.* **272**:3137-3140). CYP7A is not induced in response to cholesterol feeding in mice lacking LXR (Peet, D.J. et al. 1998 *Cell* **93**:693-704). Moreover, these animals accumulate massive amounts of cholesterol in their livers when fed a high cholesterol diet. These studies

establish LXR as a cholesterol sensor responsible for positive regulation of CYP7A expression.

[007] Bile acids stimulate the expression of genes involved in bile acid transport such as the intestinal bile acid binding protein (I-BABP) and repress CYP7A as well as other genes involved in bile acid biosynthesis such as CYP8B (which converts chenodeoxycholic acid to cholic acid), and CYP27 (which catalyzes the first step in the alternative pathway for bile acid synthesis; Javitt, N.B. 1994 *FASEB J.* **8**:1308-1311; Russell, D.W. and K.D. Setchell 1992 *Biochemistry* **31**:4737-4749). Recently, FXR was shown to be a bile acid receptor (Makishima, M. et al. 1999 *Science* **284**:1362-1365; Parks, D.J. et al. 1999 *Science* **284**:1365- 1368; Wang, H. 1999 *Mol. Cell* **3**:543-553). Several different bile acids, including chenodeoxycholic acid and its glycine and taurine conjugates were demonstrated to bind to and activate FXR at physiologic concentrations. In addition, DNA response elements for the FXR/RXR heterodimer were identified in both the human and mouse I-BABP promoters, indicating that FXR mediates positive effects of bile acids on I-BABP expression (Grober, J. et al. 1999 *J. Biol. Chem.* **274**:29749-29754; Makishima, M. et al. 1999 *Science* **284**:1362-1365). Further, the rank order of bile acids that activate FXR correlates with that for repression of CYP7A in a hepatocyte-derived cell line (Makishima, M. et al. 1999 *Science* **284**:1362-1365). Thus, these studies indicate that FXR also has a role in the negative effects of bile acids on gene expression.

[008] However, the molecular mechanism of bile acid mediated repression of CYP7A, and specifically the role of FXR in this process is unclear. Since the CYP7A promoter lacks a strong FXR/RXR binding site (Chiang, J.Y. and D. Stroup. 1994 *J. Biol. Chem.* **269**:17502-17507; Chiang, J.Y. et al. 2000 *J. Biol. Chem.* **275**:10918-10924), it is unlikely that the effect is from the direct interaction of FXR

[009] An additional nuclear receptor also involved in the expression of CYP7A is the liver receptor homolog-1 (LRH1, also called CPF, hB1F, and NR5A2), a monomeric orphan nuclear receptor that functions as a tissue specific transcription factor (Becker-Andre et al 1993 *Biochem. Biophys. Res. Comm.* **194**:1371-1379; Galarneau et al 1996 *Mol. Cell. Biol.* **16**:3853-3865; Li

et al 1998 *J. Biol. Chem.* **273**:29022-29031; Nitta et al 1999 *Proc. Natl. Acad. Sci. USA* **96**: 6660-6665). High level expression of LRH1 has been shown in the liver, pancreas, and ovary, with less abundant expression in the colon, intestine, and the adrenal gland (Nitta et al 1999 *Proc. Natl. Acad. Sci. USA* **96**: 6660-6665; Li et al 1998 *J. Biol. Chem.* **273**:29022-29031; Repa and Mangelsdorf 2000 *Ann Rev. Cell. Dev*, Wang et al 2001 *J. Mol. Endo.* **27**:255-258). Whereas the biological role for LRH-1 is still emerging, it is clear that LRH-1 is required for hepatic expression of CYP7A and maximizes this expression via synergizing with LXR (Nitta et al 1999 *Proc. Natl. Acad. Sci. USA* **96**: 6660-6665; Lu et al 2000 *Mol. Cell* **6**:507-517).

[0010] LRH1 can also induce the expression of short heterodimer partner (SHP, NR0B2), an orphan nuclear receptor that represses transcription and inhibits the function of other nuclear receptors (Seol et al 1996 *Science* **272**:1336-1339, Johansson et al 1999 *J. Biol. Chem.* **274**:345-353, Lee et al 1999 *J. Biol. Chem.* **274**:20869-20873). SHP is also a direct gene target of FXR and SHP expression is upregulated via FXR agonist compounds including the bile acid CDCA and the synthetic FXR agonist GW4064 (Lu et al 2000 *Mol. Cell* **6**:507-517, Goodwin et al 2000 *Mol. Cell* **6**: 517-526). Therefore, FXR agonists indirectly repress CYP7a via induction of the repressor SHP, which subsequently binds to and represses the transcriptional activity of LRH1 on the CYP7A promoter (Lu et al 2000 *Mol. Cell* **6**:507-517; Goodwin et al 2000 *Mol. Cell* **6**: 517-526). These finding demonstrate the existence of complex regulatory cascades involving five different nuclear receptors including FXR, RXR, LXR, LRH, and SHP, that coordinately govern bile acid synthesis and cholesterol and lipid homeostasis.

[0011] Recent findings concerning human loss of function mutations in the CYP7a locus as well as pharmacological studies describing the discovery of a naturally occurring FXR antagonist point to the potential beneficial therapeutic indications of an FXR antagonist. Studies performed by Pullinger et al (2002 *J. Clin Invest.* **110**: 109-117) show that human patients harboring a loss of function mutation in CYP7a present with a hypercholesterolemic phenotype coupled with profound resistance to HMG-CoA reductase inhibitors (also known generically as "statins"). Additionally, two independent groups have

reported that a natural product termed Guggulsterone functions as an FXR antagonist. Guggulsterone represses SHP expression and SHP-dependent repression of CYP7a, resulting in lowered LDL and triglyceride in mouse models (Urizar et al 2002 Science: 1703-1706; Wu, J. et al 2002 *Mol Endocrinol.* 16:1590-7). Given these results, any genetic or pharmacological means of elevating CYP7a expression or activity in humans would be likely to have a beneficial therapeutic effect upon cholesterol metabolism and homeostasis. For example, the ability to inhibit FXR expression and therefore FXR-dependent upregulation of SHP should prevent bile acid mediated feedback repression of CYP7a.

[0012] Despite the variety of Farnesoid X Receptor inhibitors disclosed in the art, there still remains a need for therapeutic agents capable of effectively and specifically inhibiting the function of the Farnesoid X Receptor (FXR)

[0013] Antisense technology is emerging as an effective means for reducing the expression of specific gene products and may therefore prove to be uniquely useful in a number of therapeutic, diagnostic, and research applications for the modulation of FXR expression.

SUMMARY OF THE INVENTION

[0014] The present invention is directed to antisense compounds, particularly oligonucleotides, which are targeted to a nucleic acid encoding Farnesoid X Receptor (FXR), and which modulate the expression of FXR. Pharmaceutical and other compositions comprising the antisense compounds of the invention are also provided. Further provided are methods of modulating the expression of FXR in cells or tissues comprising contacting said cells or tissues with one or more of the antisense compounds or compositions of the invention. Further provided are methods of treating an animal, particularly a human, suspected of having or being prone to a disease or condition associated with expression of FXR by administering a therapeutically or prophylactically effective amount of one or more of the antisense compounds or compositions of the invention.

DETAILED DESCRIPTION OF THE INVENTION

[0015] The present invention employs oligomeric antisense compounds, particularly oligonucleotides, for use in modulating the function of nucleic acid molecules encoding FXR, ultimately modulating the amount of FXR produced. This is accomplished by providing antisense compounds, which specifically hybridize with one or more nucleic acids encoding FXR. As used herein, the terms "target nucleic acid" and "nucleic acid encoding FXR" encompass DNA encoding FXR, RNA (including pre-mRNA and mRNA) transcribed from such DNA, and also cDNA derived from such RNA. The specific hybridization of an oligomeric compound with its target nucleic acid interferes with the normal function of the nucleic acid. This modulation of function of a target nucleic acid by compounds, which specifically hybridize to it, is generally referred to as "antisense". The functions of DNA to be interfered with include replication and transcription. The functions of RNA to be interfered with include all vital functions such as, for example, translocation of the RNA to the site of protein translation, translation of protein from the RNA, splicing of the RNA to yield one or more mRNA species, and catalytic activity which may be engaged in or facilitated by the RNA. The overall effect of such interference with target nucleic acid function is modulation of the expression of FXR. In the context of the present invention, "modulation" means either an increase (stimulation) or a decrease (inhibition) in the expression of a gene. In the context of the present invention, inhibition is the preferred form of modulation, of gene expression and mRNA is a preferred target.

[0016] It is preferred to target specific nucleic acids for antisense. "Targeting" an antisense compound to a particular nucleic acid, in the context of this invention, is a multistep process. The process usually begins with the identification of a nucleic acid sequence whose function is to be modulated. This may be, for example, a cellular gene (or mRNA transcribed from the gene) whose expression is associated with a particular disorder or disease state, or a nucleic acid molecule from an infectious agent. In the present invention, the target is a nucleic acid molecule encoding FXR. The targeting process also includes determination of a site or sites within this gene for the antisense

interaction to occur such that the desired effect, e.g., detection or modulation of expression of the protein, will result. Within the context of the present invention, a preferred intragenic site is the region encompassing the translation initiation or termination codon of the open reading frame (ORF) of the gene. Since, as is known in the art, the translation initiation codon is typically 5'-AUG (in transcribed mRNA molecules; 5'-ATG in the corresponding DNA molecule), the translation initiation codon is also referred to as the "AUG codon," the "start codon" or the "AUG start codon". A minority of genes have a translation initiation codon having the RNA sequence 5'-GUG, 5'-UUG or 5'-CUG, and 5'-AUA, 5'-ACG and 5'-CUG have been shown to function in vivo. Thus, the terms "translation initiation codon" and "start codon" can encompass many codon sequences, even though the initiator amino acid in each instance is typically methionine (in eukaryotes) or formylmethionine (in prokaryotes). It is also known in the art that eukaryotic and prokaryotic genes may have two or more alternative start codons, any one of which may be preferentially utilized for translation initiation in a particular cell type or tissue, or under a particular set of conditions. In the context of the invention, "start codon" and "translation initiation codon" refer to the codon or codons that are used in vivo to initiate translation of an mRNA molecule transcribed from a gene encoding FXR, regardless of the sequence(s) of such codons.

[0017] It is also known in the art that a translation termination codon (or "stop codon") of a gene may have one of three sequences, i.e. 5'-UAA, 5'-UAG and 5'-UGA (the corresponding DNA sequences are 5'-TAA, 5'-TAG and 5'-TGA, respectively). The terms "start codon region" and "translation initiation codon region "refer to a portion of such an mRNA or gene that encompasses from about 25 to about 50 contiguous nucleotides in either direction (i.e., 5' or 3') from a translation initiation codon. Similarly, the terms "stop codon region" and "translation termination codon region "refer to a portion of such an mRNA or gene that encompasses from about 25 to about 50 contiguous nucleotides in either direction (i.e., 5' or 3') from a translation termination codon.

[0018] The open reading frame (ORF) or "coding region," which is known in the art to refer to the region between the translation initiation codon and the translation termination codon, is also a region which may be targeted

effectively. Other target regions include the 5' untranslated region (5'UTR), known in the art to refer to the portion of an mRNA in the 5' direction from the translation initiation codon, and thus including nucleotides between the 5' cap site and the translation initiation codon of an mRNA or corresponding nucleotides on the gene, and the 3' untranslated region (3'UTR), known in the art to refer to the portion of an mRNA in the 3' direction from the translation termination codon, and thus including nucleotides between the translation termination codon and 3' end of an mRNA or corresponding nucleotides on the gene. The 5' cap of an mRNA comprises an N7-methylated guanosine residue joined to the 5'-most residue of the mRNA via a 5'-5' triphosphate linkage. The 5' cap region of an mRNA is considered to include the 5' cap structure itself as well as the first 50 nucleotides adjacent to the cap. The 5' cap region may also be a preferred target region.

[0019] Although some eukaryotic mRNA transcripts are directly translated, many contain one or more regions, known as "introns," which are excised from a transcript before it is translated. The remaining (and therefore translated) regions are known as "exons" and are spliced together to form a continuous mRNA sequence. mRNA splice sites, i.e., intron-exon junctions, may also be preferred target regions, and are particularly useful in situations where aberrant splicing is implicated in disease, or where an overproduction of a particular mRNA splice product is implicated in disease. Aberrant fusion junctions due to rearrangements or deletions are also preferred targets. It has also been found that introns can also be effective, and therefore preferred, target regions for antisense compounds targeted, for example, to DNA or pre-mRNA.

[0020] Once one or more target sites have been identified, oligonucleotides are chosen which are sufficiently complementary to the target, i.e., hybridize sufficiently well and with sufficient specificity, to give the desired effect.

[0021] In the context of this invention, "hybridization" means hydrogen bonding, which may be Watson-Crick, Hoogsteen, or reversed Hoogsteen hydrogen bonding, between complementary nucleoside or nucleotide bases. For example, adenine and thymine are complementary nucleobases, which pair through the formation of hydrogen bonds. "Complementary," as used herein, refers to the capacity for precise pairing between two nucleotides. For example,

if a nucleotide at a certain position of an oligonucleotide is capable of hydrogen bonding with a nucleotide at the same position of a DNA or RNA molecule, then the oligonucleotide and the DNA or RNA are considered to be complementary to each other at that position. The oligonucleotide and the DNA or RNA are complementary to each other when a sufficient number of corresponding positions in each molecule are occupied by nucleotides which can hydrogen bond with each other. Thus, "specifically hybridizable" and "complementary" are terms which are used to indicate a sufficient degree of complementarity or precise pairing such that stable and specific binding occurs between the oligonucleotide and the DNA or RNA target. It is understood in the art that the sequence of an antisense compound need not be 100% complementary to that of its target nucleic acid to be specifically hybridizable. An antisense compound is specifically hybridizable when binding of the compound to the target DNA or RNA molecule interferes with the normal function of the target DNA or RNA to cause a loss of utility, and there is a sufficient degree of complementarity to avoid non-specific binding of the antisense compound to non-target sequences under conditions in which specific binding is desired, i.e., under physiological conditions in the case of in vivo assays or therapeutic treatment, and in the case of in vitro assays, under conditions in which the assays are performed.

[0022] Antisense compounds are commonly used as research reagents and diagnostics. For example, antisense oligonucleotides, which are able to inhibit gene expression with exquisite specificity, are often used by those of ordinary skill to elucidate the function of particular genes. Antisense compounds are also used, for example, to distinguish between functions of various members of a biological pathway. Antisense modulation has, therefore, been harnessed for research use.

[0023] The specificity and sensitivity of antisense is also harnessed by those of skill in the art for therapeutic uses. Antisense oligonucleotides have been employed as therapeutic moieties in the treatment of disease states in animals and man. Antisense oligonucleotides have been safely and effectively administered to humans and numerous clinical trials are presently underway. It is thus established that oligonucleotides can be useful therapeutic modalities

that can be configured to be useful in treatment regimes for treatment of cells, tissues and animals, especially humans. In the context of this invention, the term "oligonucleotide" refers to an oligomer or polymer of ribonucleic acid (RNA) or deoxyribonucleic acid (DNA) or mimetics thereof. This term includes oligonucleotides composed of naturally occurring nucleobases, sugars and covalent internucleoside (backbone) linkages as well as oligonucleotides having non-naturally occurring portions which function similarly. Such modified or substituted oligonucleotides are often preferred over native forms because of desirable properties such as, for example, enhanced cellular uptake, enhanced affinity for nucleic acid target and increased stability in the presence of nucleases.

[0024] While antisense oligonucleotides are a preferred form of antisense compound, the present invention comprehends other oligomeric antisense compounds, including but not limited to oligonucleotide mimetics such as are described below. The antisense compounds in accordance with this invention preferably comprise from about 8 to about 30 nucleobases (i.e. from about 8 to about 30 linked nucleo sides). Particularly preferred antisense compounds are antisense oligonucleotides, even more preferably those comprising from about 12 to about 25 nucleobases. As is known in the art, a nucleoside is a base-sugar combination. The base portion of the nucleoside is normally a heterocyclic base. The two most common classes of such heterocyclic bases are the purines and the pyrimidines. Nucleotides are nucleosides that further include a phosphate group covalently linked to the sugar portion of the nucleoside. For those nucleosides that include a pentofuranosyl sugar, the phosphate group can be linked to either the 2', 3', or 5' hydroxyl moiety of the sugar. In forming oligonucleotides, the phosphate groups covalently link adjacent nucleosides to one another to form a linear polymeric compound. In turn the respective ends of this linear polymeric structure can be further joined to form a circular structure, however, open linear structures are generally preferred. Within the oligonucleotide structure, the phosphate groups are commonly referred to as forming the internucleoside backbone of the oligonucleotide. The normal I linkage or backbone of RNA and DNA is a 3' to 5' phosphodiester linkage.

[0025] Specific examples of preferred antisense compounds useful in this invention include oligonucleotides containing modified backbones or non-natural internucleoside linkages. As defined in this specification, oligonucleotides having modified backbones include those that retain a phosphorus atom in the backbone and those that do not have a phosphorus atom in the backbone. For the purposes of this specification, and as sometimes referenced in the art, modified oligonucleotides that do not have a phosphorus atom in their internucleoside backbone can also be considered to be oligonucleosides.

[0026] Preferred modified oligonucleotide backbones include, for example, phosphorothioates, chiral phosphorothioates, phosphorodithioates, phosphotriesters, aminoalkylphosphotriesters, methyl and other alkyl phosphonates including 3'alkylene phosphonates and chiral phosphonates, phosphinates, phosphoramidates including 3'-amino phosphoramidate and aminoalkylphosphoramidates, thionophosphoramidates, thionoalkylphosphonates, thionoalkylphosphotriesters, and boranophosphates having normal 3'-5' linkages, 2'-5' linked analogs of these, and those having inverted polarity wherein the adjacent pairs of nucleoside units are linked 3'-5' to 5'-3' or 2'-5' to 5'-2'. Various salts, mixed salts and free acid forms are also included.

[0027] Representative United States patents that teach the preparation of the above phosphorus-containing linkages include, but are not limited to, U.S. 3,687,808; 4,469,863; 4,476,301; 5,023,243; 5,177,196; 5,188,897; 5,264,423; 5,276,019; 5,278,302; 5,286,717; 5,321,131; 5,399,676; 5,405,939; 5,453,496; 5,455,233; 5,466,677; 5,476,925; 5,519,126; 5,536,821; 5,541,306; 5,550,111; 5,563,253; 5,571,799; 5,587,361; and 5,625,050, each of which is herein incorporated by reference.

[0028] Preferred modified oligonucleotide backbones that do not include a phosphorus atom therein have backbones that are formed by short chain alkyl or cycloalkyl internucleoside linkages, mixed heteroatom and alkyl or cycloalkyl internucleoside linkages, or one or more short chain heteroatomic or heterocyclic internucleoside linkages. These include those having morpholino linkages (formed in part from the sugar portion of a nucleoside); siloxane

backbones; sulfide, sulfoxide and sulfone backbones; formacetyl and thioformacetyl backbones; methylene formacetyl and thioformacetyl backbones; alkene containing backbones; sulfamate backbones; methyleneimino and methylenehydrazino backbones; sulfonate and sulfonamide baçkbones; amide backbones; and others having mixed N, O, S and CH_2 component parts.

[0029] Representative United States patents that teach the preparation of the above oligonucleosides include, but are not limited to, U.S. 5,034,506; 5,166,315; 5,185,444; 5,214,134; 5,216,141; 5,235,033; 5,264,562; 5,264,564; 5,405,938; 5,434,257; 5,466,677; 5,470,967; 5,489,677; 5,541,307; 5,561,225; 5,596,086; 5,602,240; 5,610,289; 5,602,240; 5,608,046; 5,610,289; 5,618,704; 5,623,070; 5,663,312; 5,633,360; 5,677,437; and 5,677,439, ach of which is herein incorporated by reference.

[0030] In other preferred oligonucleotide mimetics, both the sugar and the internucleoside linkage, i.e., the backbone, of the nucleotide units are replaced with novel groups. The base units are maintained for hybridization with an appropriate nucleic acid target compound. One such oligomeric compound, an oligonucleotide mimetic that has been shown to have excellent hybridization properties, is referred to as a peptide nucleic acid (PNA). In PNA compounds, the sugar-backbone of an oligonucleotide is replaced with an amide containing backbone, in particular an aminoethylglycine backbone. The nucleobases are retained and are bound directly or indirectly to aza nitrogen atoms of the amide portion of the backbone. Representative United States patents that teach the preparation of PNA compounds include, but are not limited to, U.S. 5,539,082; 5,714,331; and 5,719,262, each of which is herein incorporated by reference. Further teaching of PNA compounds can be found in Nielsen et al. (*Science*, 1991, 254, 1497-1500).

[0031] Most preferred embodiments of the invention are oligonucleotides with phosphorothioate backbones and oligonucleosides with heteroatom backbones, and in particular $-CH_2-NH-O-CH_2-$, $-CH_2-N(CH_3)-O-CH_2-$ [known as a methylene (methylimino) or MMI backbone], $-CH_2-O-N(CH_3)-CH_2-$, $-CH_2N(CH_3)-N(CH_3)-CH_2-$ and $-O-N(CH_3)-CH_2-CH_2-$ [wherein the native phosphodiester backbone is represented as $-O-P-O-CH_2-$] of the above referenced U.S. patent 5,489,677, and the amide backbones of the above

referenced U.S. patent 5,602,240. Also preferred are oligonucleotides having morpholino backbone structures of the above-referenced U.S. patent 5,034,506.

[0032] Modified oligonucleotides may also contain one or more substituted sugar moieties. Preferred oligonucleotides comprise one of the following at the 2' position: OH; F; O-, S-, or N-alkyl; O-, S-, or N-alkenyl; O-, S- or N-alkynyl; or O-alkyl-O-alkyl, wherein the alkyl, alkenyl and alkynyl may be substituted or unsubstituted C_1 to C_{10} alkyl or C_2 to C_{10} alkenyl and alkynyl. Particularly preferred are $O[(CH_2)_nO]_mCH_3$, $O(CH_2)_n$,OCH_3, $O(CH_2)_nNH_2$, $O(CH_2)_nCH_3$, $O(CH_2)_nONH_2$, and $O(CH_{2n}ON[(CH_2)_nCH_3)]_2$ where n and m are from 1 to about 10. Other preferred oligonucleotides comprise one of the following at the 2' position: C_1 to C_{10}, (lower alkyl, substituted lower alkyl, alkaryl, aralkyl, O-alkaryl or O-aralkyl, SH, SCH_3, OCN, Cl, Br, CN, CF_3, OCF_3, $SOCH_3$, SO_2CH_3, ONO_2, NO_2, N_3, NH_2, heterocycloalkyl, heterocycloalkaryl, aminoalkylamino, polyalkylamino, substituted silyl, an RNA cleaving group, a reporter group, an intercalator, a group for improving the pharmacokinetic properties of an oligonucleotide, or a group for improving the pharmacodynamic properties of an oligonucleotide, and other substituents having similar properties. A preferred modification includes 2' -methoxyethoxy (2' -O-$CH_2CH_2OCH_3$, also known as 2'-O- (2-methoxyethyl) or 2'-MOE) (Martin et al., *Helv. Chim. Acta*, 1995, 78, 486-504) i.e., an alkoxyalkoxy group. A further preferred modification includes 2'-dimethylaminooxyethoxy, i.e., a $O(CH_2)_2ON(CH_3)_2$ group, also known as 2'-DMAOE, as described in examples herein below, and 2'-dimethylaminoethoxyethoxy (also known in the art as 2'-O-dimethylaminoethoxyethyl or 2'-DMAEOE), i.e., 2'-O-CH_2-O-CH_2-N $(CH_2)_2$, also described in examples herein below.

[0033] Other preferred modifications include 2'-methoxy (2'-O CH_3), 2'-aminopropoxy (2'-O CH_2 CH_2 CH_2NH_2), and 2'-fluoro (2'-F). Similar modifications may also be made at other positions on the oligonucleotide, particularly the 3' position of the sugar on the 3' terminal nucleotide or in 2'-5' linked oligonucleotides and the 5' position of 5' terminal nucleotide. Oligonucleotides may also have sugar mimetics such as cyclobutyl moieties in place of the pentofuranosyl sugar. Representative United States patents that teach the preparation of such modified sugar structures include, but are not

limited to, U.S. 4,981,957; 5,118,800; 5,319,080; 5,359,044; 5,393,878; 5,446,137; 5,466,786; 5,514,785; 5,519,134; 5,567,811; 5,576,427; 5,591,722; 5,597,909; 5,610,300; 5,627,053; 5,639,873; 5,646,265; 5,658,873; 5,670,633; and 5,700,920, each of which is herein incorporated by reference in its entirety.

[0034] Oligonucleotides may also include nucleobase (often referred to in the art simply as "base") modifications or substitutions. As used herein, "unmodified" or "natural" nucleobases include the purine bases adenine (A) and guanine (G), and the pyrimidine bases thymine (T), cytosine (C) and uracil (U). Modified nucleobases include other synthetic and natural nucleobases such as 5-methylcytosine (5-me-C), 5-hydroxymethyl cytosine, xanthine, hypoxanthine, 2-aminoadenine, 6-methyl and other alkyl derivatives of adenine and guanine, 2-propyl and other alkyl derivatives of adenine and guanine, 2-thiouracil, 2-thiothymine and 2-thiocytosine, 5-halouracil and cytosine, 5-propynyl uracil and cytosine, 6-azo uracil, cytosine and thymine, 5-uracil (pseudouracil), 4-thiouracil, 8-halo, 8-amino, 8-thiol, 8-thioalkyl, 8-hydroxyl and other 8-substituted adenines and guanines, 5-halo particularly 5-bromo, 5-trifluoromethyl and other 5-substituted uracils and cytosines, 7-methylquanine and 7-methyladenine, 8-azaguanine and 8-azaadenine, 7-deazaguanine and 7-deazaadenine and 3-deazaguanine and 3-deazaadenine. Further nucleobases include those disclosed in United States Patent No. 3,687,808, those disclosed in *The Concise Encyclopedia Of Polymer Science And Engineering*, pages 858-859, Kroschwitz, J.I., ed. John Wiley & Sons, 1990, those disclosed by Englisch et al., *Angewandte Chemie*, International Edition, 1991, 30, 613, and those disclosed by Sanghvi, Y.S., Chapter 15, *Antisense Research and Applications*, pages 289-302, Crooke, S.T. and Lebleu, B. ed., CRC Press, 1993. Certain of these nucleobases are particularly useful for increasing the binding affinity of the oligomeric compounds of the invention. These include 5-substituted pyrimidines, 6-azapyrimidines and N-2, N-6 and O-6 substituted purines, including 2-aminopropyladenine, 5-propynyluracil and 5-propynylcytosine. 5-methylcytosine substitutions have been shown to increase nucleic acid duplex stability by 0.6-1.2°C (Sanghvi, Y.S., Crooke, S.T. and Lebleu, B., eds, *Antisense Research and Applications*, CRC Press, Boca Raton, 1993, pp. 276-

278) and are presently preferred base substitutions, even more particularly when combined with 2'-O-methoxyethyl sugar modifications.

[0035] Representative United States patents that teach the preparation of certain of the above noted modified nucleobases as well as other modified nucleobases include, but are not limited to, the above noted U.S. 3,687,808, as well as U.S. 4,845,205; 5,130,302; 5,134,066; 5,175,273; 5,367,066; 5,432,272; 5,457,187; 5,459,255; 5,484,908; 5,502,177; 5,525,711; 5,552,540; 5,587,469; 5,594,12', 5,596,091; 5,614,617; 5,750,692, and 5,681,941, each of which is herein incorporated by reference.

[0036] Another modification of the oligonucleotides of the invention involves chemically linking to the oligonucleotide one or more moieties or conjugates, which enhance the activity, cellular distribution, or cellular uptake of the oligonucleotide. Such moieties include but are not limited to lipid moieties such as a cholesterol moiety (Letsinger et al., *Proc. Natl. Acad. Sci. USA*, 1989, 86, 6553-6556), cholic acid (Manoharan et al., *Bioorg. Med. Chem. Let.*, 1994, 4, 1053-1060), a thioether, e.g., hexyl-S-tritylthiol (Manoharan et al., *Ann. N.Y. Acad. Sci.*, 1992, 660, 306-309; Manoharan et al., *Bioorg. Med. Chem. Let.*, 1993, 3, 2765-2770), a thiocholesterol (Oberhauser et al., *Nucl. Acids Res.*, 1992, 20, 533-538), an aliphatic chain, e.g., dodecandiol or undecyl residues (Saison-Behmoaras et al., *EMBO J.*, 1991, 10, 1111-1118; Kabanov et al., *FEBS Lett.*, 1990, 259, 327-330; Svinarchuk et al., *Biochimie*, 1993, 75, 49-54), a phospholipid, e.g., di-hexadecyl-rac-glycerol or triethylammonium 1,2-di-O-hexadecyl-rac-glycero-3-H-phosphonate (Manoharan et al., *Tetrahedron Lett.*, 1995, 36, 3651-3654; Shea et al., *Nucl. Acids Res.*, 1990, 18, 3777-3783), a polyamine or a polyethylene glycol chain (Mancharan et al., *Nucleosides & Nucleotides*, 1995, 14, 969-973), or adamantane acetic acid (Manoharan et al., *Tetrahedron Lett.*, 1995, 36, 3651-3654), a palmityl moiety (Mishra et al., *Biochim. Biophys. Acta*, 1995, 1264, 229-237), or an octadecylamine or hexylamino-carbonyl-oxycholesterol moiety (Crooke et al., *J. Pharmacol. Exp. Ther.*, 1996, 277, 923-937).

[0037] Representative United States patents that teach the preparation of such oligonucleotide conjugates include, but are not limited to, U.S. 4,828,979; 4,948,882; 5,218,105; 5,525,465; 5,541,313; 5,545,730; 5,552,538; 5,578,717,

5,580,731; 5,580,731; 5,591,584; 5,109,124; 5,118,802; 5,138,045; 5,414,077; 5,486,603; 5,512,439; 5,578,718; 5,608,046; 4,587,044; 4,605,735; 4,667,025; 4,762,779; 4,789,737; 4,824,941; 4,835,263; 4,876,335; 4,904,582; 4,958,013; 5,082,830; 5,112,963; 5,214,136; 5,082,830; 5,112,963; 5,214,136; 5,245,022; 5,254,469; 5,258,506; 5,262,536; 5,272,250; 5,292,873; 5,317,098; 5,371,241, 5,391,723; 5,416,203, 5,451,463; 5,510,475; 5,512,667; 5,514,785; 5,565,552; 5,567,810; 5,574,142; 5,585,481; 5,587,371; 5,595,726; 5,597,696; 5,599,923; 5,599,928 and 5,688,941, each of which is herein incorporated by reference.

[0038] It is not necessary for all positions in a given compound to be uniformly modified, and in fact more than one of the aforementioned modifications may be incorporated in a single compound or even at a single nucleoside within an oligonucleotide. The present invention also includes antisense compounds, which are chimeric compounds. "Chimeric" antisense compounds or "chimeras," in the context of this invention, are antisense compounds, particularly oligonucleotides, which contain two or more chemically distinct regions, each made up of at least one monomer unit, i.e., a nucleotide in the case of an oligonucleotide compound. These oligonucleotides typically contain at least one region wherein the oligonucleotide is modified so as to confer upon the oligonucleotide increased resistance to nuclease degradation, increased cellular uptake, and/or increased binding affinity for the target nucleic acid. An additional region of the oligonucleotide may serve as a substrate for enzymes capable of cleaving RNA:DNA or RNA:RNA hybrids. By way of example, RNase H is a cellular endonuclease, which cleaves the RNA strand of RNA:DNA duplex. Activation of RNase H, therefore, results in cleavage of the RNA target, thereby greatly enhancing the efficiency of oligonucleotide inhibition of gene expression. Consequently, comparable results can often be obtained with shorter oligonucleotides when chimeric oligonucleotides are used, compared to phosphorothioate deoxyoligonucleotides hybridizing to the same target region. Cleavage of the RNA target can be routinely detected by gel electrophoresis and, if necessary, associated nucleic acid hybridization techniques known in the art.

[0039] Chimeric antisense compounds of the invention may be formed as composite structures of two or more oligonucleotides, modified

oligonucleotides, oligonucleosides and/or oligonucleotide mimetics as described above. Such compounds have also been referred to in the art as hybrids or gapmers. Representative United States patents that teach the preparation of such hybrid structures include, but are not limited to, U.S. 5,013,830; 5,149,797; 5,220,007; 5,256,775; 5,366,878; 5,403,711; 5,491,133; 5,565,350; 5,623,065; 5,652,355; 5,652,356; and 5,700,922, each of which is herein incorporated by reference in its entirety.

[0040] The antisense compounds used in accordance with this invention may be conveniently, and routinely made through the well-known technique of solid phase synthesis. Equipment for such synthesis is sold by several vendors including, for example, Applied Biosystems (Foster City, CA). Any other means for such synthesis known in the art may additionally or alternatively be employed. It is well known to use similar techniques to prepare oligonucleotides such as the phosphorothioates and alkylated derivatives.

[0041] The antisense compounds of the invention are synthesized in vitro and do not include antisense compositions of biological origin, or genetic vector constructs designed to direct the in vivo synthesis of antisense molecules. The compounds of the invention may also be admixed, encapsulated, conjugated or otherwise associated with other molecules, molecule structures or mixtures of compounds, as for example, liposomes, receptor targeted molecules, oral, rectal, topical or other formulations, for assisting in uptake, distribution and/or absorption. Representative United States patents that teach the preparation of such uptake, distribution and/or absorption assisting formulations include, but are not limited to, U.S. 5,108,921; 5,354,844; 5,416,016; 5,459,127; 5,521,291; 5,543,158; 5,547,932; 5,583,020; 5,591,721; 4,426,330; 4,534,899; 5,013,556; 5,108,921; 5,213,804; 5,227,170; 5,264,221; 5,356,633; 5,395,619; 5,416,016; 5,417,978; 5,462,854; 5,469,854; 5,512,295; 5,527,528; 5,534,259; 5,543,152; 5,556,948; 5,580,575; and 5,595,756, each of which is herein incorporated by reference.

[0042] The antisense compounds of the invention encompass any pharmaceutically acceptable salts, esters, or salts of such esters, or any other compound which, upon administration to an animal including a human, is capable of providing (directly or indirectly) the biologically active metabolite or

residue thereof. Accordingly, for example, the disclosure is also drawn to prodrugs and pharmaceutically acceptable salts of the compounds of the invention, pharmaceutically acceptable salts of such prodrugs, and other bioequivalents.

[0043] The term "prodrug" indicates a therapeutic agent that is prepared in an inactive form that is converted to an active form (i.e., drug) within the body or cells thereof by the action of endogenous enzymes or other chemicals and/or conditions. In particular, prodrug versions of the oligonucleotides of the invention are prepared as SATE [(S-acetyl-2-thioethyl) phosphate] derivatives according to the methods disclosed in WO 93/24510 to Gosselin et al., published December 9, 1993 or in WO 94/26764 to Imbach et al.

[0044] The term "pharmaceutically acceptable salts" refers to physiologically and pharmaceutically acceptable salts of the compounds of the invention: i.e., salts that retain the desired biological activity of the parent compound and do not impart undesired toxicological effects thereto.

[0045] Pharmaceutically acceptable base addition salts are formed with metals or amines, such as alkali and alkaline earth metals or organic amines. Examples of metals used as cations are sodium, potassium, magnesium, calcium, and the like. Examples of suitable amines are N, N'-dibenzylethylenediamine, chloroprocaine, choline, diethanolamine, dicyclohexylamine, ethylenediamine, N-methylglucamine, and procaine (see, for example, Berge et al., "Pharmaceutical Salts," *J. of Pharma Sci.*, 1977, 66, 119). The base addition salts of said acidic compounds are prepared by contacting the free acid form with a sufficient amount of the desired base to produce the salt in the conventional manner. The free acid form may be regenerated by contacting the salt form with an acid and isolating the free acid in the conventional manner. The free acid forms differ from their respective salt forms somewhat in certain physical properties such as solubility in polar solvents, but otherwise the salts are equivalent to their respective free acid for purposes of the present invention. As used herein, a "pharmaceutical addition salt" includes a pharmaceutically acceptable salt of an acid form of one of the components of the compositions of the invention. These include organic or inorganic acid salts of the amines. Preferred acid salts are the hydrochlorides,

acetates, salicylates, nitrates, and phosphates. Other suitable pharmaceutically acceptable salts are well known to those skilled in the art and include basic salts of a variety of inorganic and organic acids, such as, for example, with inorganic acids, such as for example hydrochloric acid, hydrobromic acid, sulfuric acid or phosphoric acid; with organic carboxylic, sulfonic, sulfo or phospho acids or N-substituted sulfamic acids, for example acetic acid, propionic acid, glycolic acid, succinic acid, maleic acid, hydroxymaleic acid, methylmaleic acid, fumaric acid, malic acid, tartaric acid, lactic acid, oxalic acid, gluconic acid, glucaric acid, glucuronic acid, citric acid, benzoic acid, cinnamic acid, mandelic acid, salicylic acid, 4-aminosalicylic acid, 2-phenoxybenzoic acid, 2-acetoxybenzoic acid, embonic acid, nicotinic acid or isonicotinic acid; and with amino acids, such as the 20 alpha-amino acids involved in the synthesis of proteins in nature, for example glutamic acid or aspartic acid, and also with phenylacetic acid, methanesulfonic acid, ethanesulfonic acid, 2-hydroxyethanesulfonic acid, ethane-1,2-disulfonic acid, benzenesulfonic acid, 4-methylbenzenesulfoic acid, naphthalene-2-sulfonic acid, naphthalene-1,5-disulfonic acid, 2- or 3-phosphoglycerate, glucose-6-phosphate, N-cyclohexylsulfamic acid (with the formation of cyclamates), or with other acid organic compounds, such as ascorbic acid. Pharmaceutically acceptable salts of compounds may also be prepared with a pharmaceutically acceptable cation. Suitable pharmaceutically acceptable cations are well known to those skilled in the art and include alkaline, alkaline earth, ammonium, and quaternary ammonium cations. Carbonates or hydrogen carbonates are also possible.

[0046] For oligonucleotides, preferred examples of pharmaceutically acceptable salts include but are not limited to (a) salts formed with cations such as sodium, potassium, ammonium, magnesium, calcium, polyamines such as spermine and spermidine, etc.; (b) acid addition salts formed with inorganic acids, for example hydrochloric acid, hydrobromic acid, sulfuric acid, phosphoric acid, nitric acid and the like; (c) salts formed with organic acids such as, for example, acetic acid, oxalic acid, tartaric acid, succinic acid, maleic acid, fumaric acid, gluconic acid, citric acid, malic acid, ascorbic acid, benzoic acid, tannic acid, palmitic acid, alginic acid, polyglutamic acid, naphthalenesulfonic acid, methanesulfonic acid, p-toluenesulfonic acid,

naphthalenedisulfonic acid, polygalacturonic acid, and the like; and (d) salts formed from elemental anions such as chlorine, bromine, and iodine.

[0047] The antisense compounds of the present invention can be utilized for diagnostics, therapeutics, prophylaxis, and as research reagents and kits. For therapeutics, an animal, preferably a human, suspected of having a disease or disorder, which can be treated by modulating the expression of FXR, is treated by administering antisense compounds in accordance with this invention. The compounds of the invention can be utilized in pharmaceutical compositions by adding an effective amount of an antisense compound to a suitable pharmaceutically acceptable diluent or carrier. Use of the antisense compounds and methods of the invention may also be useful prophylactically, e.g., to prevent or delay infection, inflammation, or tumor formation, for example.

[0048] The antisense compounds of the invention are useful for research and diagnostics, because these compounds hybridize to nucleic acids encoding FXR, enabling sandwich and other assays to easily be constructed to exploit this fact. Hybridization of the antisense oligonucleotides of the invention with a nucleic acid encoding FXR can be detected by means known in the art. Such means may include conjugation of an enzyme to the oligonucleotide, radiolabelling of the oligonucleotide or any other suitable detection means. Kits using such detection means for detecting the level of FXR in a sample may also be prepared.

[0049] The present invention also includes pharmaceutical compositions and formulations, which include the antisense compounds of the invention. The pharmaceutical compositions of the present invention may be administered in a number of ways depending upon whether local or systemic treatment is desired and upon the area to be treated. Administration may be topical (including ophthalmic and to mucous membranes including vaginal and rectal delivery), pulmonary, e.g., by inhalation or insufflation of powders or aerosols, including by nebulizer, intratracheal, intranasal, epidermal and transdermal), oral or parenteral. Parenteral administration includes intravenous, intraarterial, subcutaneous, intraperitoneal or intramuscular injection or infusion; or intracranial, e.g., intrathecal or intraventricular, administration.

Oligonucleotides with at least one 2'-O-methoxyethyl modification are believed to be particularly useful for oral administration.

[0050] Pharmaceutical compositions and formulations for topical administration may include transdermal patches, ointments, lotions, creams, gels, drops, suppositories, sprays, liquids, and powders. Conventional pharmaceutical carriers, aqueous, powder or oily bases, thickeners and the like may be necessary or desirable. Coated condoms, gloves, and the like may also be useful.

[0051] Compositions and formulations for oral administration include powders or granules, suspensions, or solutions in water or non-aqueous media, capsules, sachets, or tablets. Thickeners, flavoring agents, diluents, emulsifiers, dispersing aids, or binders may be desirable.

[0052] Compositions and formulations for parenteral, intrathecal or intraventricular administration may include sterile aqueous solutions, which may also contain buffers, diluents and other suitable additives such as, but not limited to, penetration enhancers, carrier compounds and other pharmaceutically acceptable carriers or excipients.

[0053] Pharmaceutical compositions of the present invention include, but are not limited to, solutions, emulsions, and liposome-containing formulations. These compositions may be generated from a variety of components that include, but are not limited to, preformed liquids, self-emulsifying solids and self-emulsifying semisolids.

[0054] The pharmaceutical formulations of the present invention, which may conveniently be presented in unit dosage form, may be prepared according to conventional techniques well known in the pharmaceutical industry. Such techniques include the step of bringing into association the active ingredients with the pharmaceutical carrier(s) or excipient(s). In general the formulations are prepared by uniformly and intimately bringing into association the active ingredients with liquid carriers or finely divided solid carriers or both, and then, if necessary, shaping the product.

[0055] The compositions of the present invention may be formulated into any of many possible dosage forms such as, but not limited to, tablets, capsules, liquid syrups, soft gels, suppositories, and enemas. The compositions of the

present invention may also be formulated as suspensions in aqueous, non-aqueous or mixed media. Aqueous suspensions may further contain substances, which increase the viscosity of the suspension including, for example, sodium carboxymethylcellulose, sorbitol, and/or dextran. The suspension may also contain stabilizers.

[0056] In one embodiment of the present invention the pharmaceutical compositions may be formulated and used as foams. Pharmaceutical foams include formulations such as, but not limited to, emulsions, microemulsions, creams, jellies, and liposomes. While basically similar in nature these formulations vary in the components and the consistency of the final product. The preparation of such compositions and formulations is generally known to those skilled in the pharmaceutical and formulation arts and may be applied to the formulation of the compositions of the present invention. Emulsions

[0057] The compositions of the present invention may be prepared and formulated as emulsions. Emulsions are typically heterogenous systems of one liquid dispersed in another in the form of droplets usually exceeding 0.1 μm in diameter. (Idson, in *Pharmaceutical Dosage Forms*, Lieberman, Rieger and Banker (Eds.), 1988, Marcel Dekker, Inc., New York, N.Y., volume 1, p. 199; Rosoff, in *Pharmaceutical Dosage Forms*, Lieberman, Rieger and Banker (Eds.), 1988, Marcel Dekker, Inc., New York, N.Y., Volume 1, p. 245; Block in *Pharmaceutical Dosage Forms*, Lieberman, Rieger and Banker (Eds.), 1988, Marcel Dekker, Inc., New York, N.Y., volume 2, p. 335; Higuchi et al., in *Remington's Pharmaceutical Sciences*, Mack Publishing Co., Easton, PA, 1985, p. 301). Emulsions are often biphasic systems comprising of two immiscible liquid phases intimately mixed and dispersed with each other. In general, emulsions may be either water-in-oil (w/o) or of the oil-in-water (o/w) variety. When an aqueous phase is finely divided into and dispersed as minute droplets into a bulk oily phase the resulting composition is called a water-in-oil (w/o) emulsion. Alternatively, when an oily phase is finely divided into and dispersed as minute droplets into a bulk aqueous phase the resulting composition is called an oil-in-water (o/w) emulsion. Emulsions may contain additional components in addition to the dispersed phases and the active drug, which may be present as a solution in either the aqueous phase, oily phase or itself as a separate phase.

Pharmaceutical excipients such as emulsifiers, stabilizers, dyes, and anti-oxidants may also be present in emulsions as needed. Pharmaceutical emulsions may also be multiple emulsions that are comprised of more than two phases such as, for example, in the case of oil-in-water-in-oil (o/w/o) and water-in-oil-in-water (w/o/w) emulsions. Such complex formulations often provide certain advantages that simple binary emulsions do not. Multiple emulsions in which individual oil droplets of an o/w emulsion enclose small water droplets constitute a w/o/w emulsion. Likewise a system of oil droplets enclosed in globules of water stabilized in an oily continuous provides an o/w/o emulsion.

[0058] Emulsions are characterized by little or no thermodynamic stability. Often, the dispersed or discontinuous phase of the emulsion is well dispersed into the external or continuous phase and maintained in this form through the means of emulsifiers or the viscosity of the formulation. Either of the phases of the emulsion may be a semisolid or a solid, as is the case of emulsion-style ointment bases and creams. Other means of stabilizing emulsions entail the use of emulsifiers that may be incorporated into either phase of the emulsion. Emulsifiers may broadly be classified into four categories: synthetic surfactants, naturally occurring emulsifiers, absorption bases, and finely dispersed solids (Idson, in *Pharmaceutical Dosaqe Forms*, Lieberman, Rieger and Banker (Eds.), 1988, Marcel Dekker, Inc., New York, N.Y., volume 1, p. 199).

[0059] Synthetic surfactants, also known as surface active agents, have found wide applicability in the formulation of emulsions and have been reviewed in the literature (Rieger, in *Pharmaceutical Dosage Forms*, Lieberman, Rieger and Banker (Eds.), 1988, Marcel Dekker, Inc., New York, N.Y., volume 1, p. 285; Idson, in *Pharmaceutical Dosage Forms*, Lieberman, Rieger and Banker (Eds.), Marcel Dekker, Inc., New York, N.Y., 1988, volume 1, p. 199). Surfactants are typically amphiphilic and comprise a hydrophilic and a hydrophobic portion. The ratio of the hydrophilic to the hydrophobic nature of the surfactant has been termed the hydrophile/lipophile balance (HLB) and is a valuable tool in categorizing and selecting surfactants in the preparation of formulations. Surfactants may be classified into different classes based on the nature of the hydrophilic group: nonionic, anionic, cationic, and amphoteric

(Rieger, in *Pharmaceutical Dosage Forms*, Lieberman, Rieger and Banker (Eds.), 1988, Marcel Dekker, Inc., New York, N.Y., volume 1, p. 285).

[0060] Naturally occurring emulsifiers used in emulsion formulations include lanolin, beeswax, phosphatides, lecithin, and acacia. Absorption bases possess hydrophilic properties such that they can soak up water to form w/o emulsions yet retain their semisolid consistencies, such as anhydrous lanolin and hydrophilic petrolatum. Finely divided solids have also been used as good emulsifiers especially in combination with surfactants and in viscous preparations. These include polar inorganic solids, such as heavy metal hydroxides, nonswelling clays such as bentonite, attapulgite, hectorite, kaolin, montmorillonite, colloidal aluminum silicate and colloidal magnesium aluminum silicate, pigments and nonpolar solids such as carbon or glyceryl tristearate.

[0061] A large variety of non-emulsifying materials are also included in emulsion formulations and contribute to the properties of emulsions. These include fats, oils, waxes, fatty acids, fatty alcohols, fatty esters, humectants, hydrophilic colloids, preservatives, and antioxidants (Block, in *Pharmaceutical Dosage Forms*, Lieberman, Rieger and Banker (Eds.), 1988, Marcel Dekker, Inc., New York, N.Y., volume 1, p. 335; Idson, in *Pharmaceutical Dosage Forms*, Lieberman, Rieger and Banker (Eds.), 1988, Marcel Dekker, Inc., New York, N.Y., volume 1, p. 199).

[0062] Hydrophilic colloids or hydrocolloids include naturally occurring gums and synthetic polymers such as polysaccharides (for example, acacia, agar, alginic acid, carrageenan, guar gum, karaya gum, and tragacanth), cellulose derivatives (for example, carboxymethylcellulose and carboxypropylcellulose), and synthetic polymers (for example, carbomers, cellulose ethers, and carboxyvinyl polymers). These disperse or swell in water to form colloidal solutions that stabilize emulsions by forming strong interfacial films around the dispersed phase droplets and by increasing the viscosity of the external phase.

[0063] Since emulsions often contain a number of ingredients such as carbohydrates, proteins, sterols, and phosphatides that may readily support the growth of microbes, these formulations often incorporate preservatives.

Commonly used preservatives included in emulsion formulations include methyl paraben, propyl paraben, quaternary ammonium salts, benzalkonium chloride, esters of p-hydroxybenzoic acid, and boric acid. Antioxidants are also commonly added to emulsion formulations to prevent deterioration of the formulation. Antioxidants used may be free radical scavengers such as tocopherols, alkyl gallate, butylated hydroxyanisole, butylated hydroxytoluene, or reducing agents such as ascorbic acid and sodium metabisulfite, and antioxidant synergists such as citric acid, tartaric acid, and lecithin.

[0064] The application of emulsion formulations via dermatological, oral, and parenteral routes and methods for their manufacture have been reviewed in the literature (Idson, in *Pharmaceutical Dosage Forms*, Lieberman, Rieger and Banker (Eds.), 1988, Marcel Dekker, Inc., New York, N.Y., volume 1, p. 199). Emulsion formulations for oral delivery have been very widely used because of reasons of ease of formulation, efficacy from an absorption and bioavailability standpoint. (Rosoff, in *Pharmaceutical Dosage Forms*, Lieberman, Rieger and Banker (Eds.), 1988, Marcel Dekker, Inc., New York, N.Y., volume 1, p. 245; Idson, in *Pharmaceutical Dosage Forms*, Lieberman, Rieger and Banker (Eds.), 1988, Marcel Dekker, Inc., New York, N.Y., volume 1, p. 199). Mineral-oil base laxatives, oil-soluble vitamins, and high fat nutritive preparations are among the materials that have commonly been administered orally as o/w emulsions.

[0065] In one embodiment of the present invention, the compositions of oligonucleotides and nucleic acids are formulated as microemulsions. A microemulsion may be defined as a system of water, oil, and amphiphile, which is a single optically isotropic, and thermodynamically stable liquid solution (Rosoff, in *Pharmaceutical Dosage Forms*, Lieberman, Rieger and Banker (Eds.), 1988, Marcel Dekker, Inc., New York, N.Y., volume 1, p. 245). Typically microemulsions are systems that are prepared by first dispersing an oil in an aqueous surfactant solution and then adding a sufficient amount of a fourth component, generally an intermediate chain-length alcohol to form a transparent system. Therefore, microemulsions have also been described as thermodynamically stable, isotropically clear dispersions of two immiscible liquids that are stabilized by interfacial films of surface-active molecules

(Leung and Shah, in: *Controlled Release of Drugs: Polymers and Aggregate Systems*, Rosoff, M., Ed., 1989, VCH Publishers, New York, pages 1852-5). Microemulsions commonly are prepared via a combination of three to five components that include oil, water, surfactant, cosurfactant, and electrolyte. Whether the microemulsion is of the water-in-oil (w/o) or an oil-in-water (o/w) type is dependent on the properties of the oil and surfactant used and on the structure and geometric packing of the polar heads and hydrocarbon tails of the surfactant molecules (Schott, in *Remington's Pharmaceutical Sciences*, Mack Publishing Co., Easton, PA, 1985, p. 271).

[0066] The phenomenological approach utilizing phase diagrams has been extensively studied and has yielded a comprehensive knowledge, to one skilled in the art, of how to formulate microemulsions (Rosoff, in *Pharmaceutical Dosage Forms*, Lieberman, Rieger and Banker (Eds.), 1988, Marcel Dekker, Inc., New York, N.Y., volume 1, p. 245; Block, in *Pharmaceutical Dosage Forms*, Lieberman, Rieger and Banker (Eds.), 1988, Marcel Dekker, Inc., New York, N.Y., volume 1, p. 335). Compared to conventional emulsions, microemulsions offer the advantage of solubilizing water-insoluble drugs in a formulation of thermodynamically stable droplets that are formed spontaneously.

[0067] Surfactants used in the preparation of microemulsions include, but are not limited to, ionic surfactants, non-ionic surfactants, Brij 96, polyoxyethylene oleyl ethers, polyglycerol fatty acid esters, tetraglycerol monolaurate (ML310), tetraglycerol monooleate (MO310), hexaglycerol monooleate (PO310), hexaglycerol pentaoleate (PO500), decaglycerol monocaprate (MCA750), decaglycerol monooleate (MO750), decaglycerol sequioleate (S0750), decaglycerol decaoleate (DAO750), alone or in combination with cosurfactants. The cosurfactant, usually a short-chain alcohol such as ethanol, 1-propanol, and 1-butanol, serves to increase the interfacial fluidity by penetrating into the surfactant film and consequently creating a disordered film because of the void space generated among surfactant molecules. Microemulsions may, however, be prepared without the use of cosurfactants and alcohol-free self-emulsifying microemulsion systems are known in the art. The aqueous phase may typically be, but is not limited to,

water, an aqueous solution of the drug, glycerol, PEG300, PEG400, polyglycerols, propylene glycols, and derivatives of ethylene glycol. The oil phase may include, but is not limited to, materials such as Captex 300, Captex 355, Capmul MCM, fatty acid esters, medium chain (C8-C12) mono, di, and triglycerides, polyoxyethylated glyceryl fatty acid esters, fatty alcohols, polyglycolized glycerides, saturated polyglycolized C8-C10 glycerides, vegetable oils and silicone oil.

[0068] Microemulsions are particularly of interest from the standpoint of drug solubilization and the enhanced absorption of drugs. Lipid based microemulsions (both o/w and w/o) have been proposed to enhance the oral bioavailability of drugs, including peptides (Constantinides et al., *Pharmaceutical Research*, 1994, 11, 1385-1390; Ritschel, *Meth. Find. Exp. Clin. Pharmacol.*, 1993, 13, 205). Microemulsions afford advantages of improved drug solubilization, protection of drug from enzymatic hydrolysis, possible enhancement of drug absorption due to surfactant-induced alterations in membrane fluidity and permeability, ease of preparation, ease of oral administration over solid dosage forms, improved clinical potency, and decreased toxicity (Constantinides et al., *Pharmaceutical Research*, 1994, 11, 1385; Ho et al., *J. Pharm. Sci.*, 1996, 85, 138-143). Often microemulsions may form spontaneously when their components are brought together at ambient temperature. This may be particularly advantageous when formulating thermolabile drugs, peptides, or oligonucleotides. Microemulsions have also been effective in the transdermal delivery of active components in both cosmetic and pharmaceutical applications. It is expected that the microemulsion compositions and formulations of the present invention will facilitate the increased systemic absorption of oligonucleotides and nucleic acids from the gastrointestinal tract, as well as improve the local cellular uptake of oligonucleotides and nucleic acids within the gastrointestinal tract, vagina, buccal cavity and other areas of administration.

[0069] Microemulsions of the present invention may also contain additional components and additives such as sorbitan monostearate (Grill 3), Labrasol, and penetration enhancers to improve the properties of the formulation and to enhance the absorption of the oligonucleotides and nucleic acids of the present

invention. Penetration enhancers used in the microemulsions of the present invention may be classified as belonging to one of five broad categories - surfactants, fatty acids, bile salts, chelating agents, and non-chelating non-surfactants (Lee et al., *Critical Reviews in Therapeutic Drug Carrier Systems*, 1991, p. 92). Each of these classes has been discussed above.

Liposomes

[0070] There are many organized surfactant structures besides microemulsions that have been studied and used for the formulation of drugs. These include monolayers, micelles, bilayers, and vesicles. Vesicles, such as liposomes, have attracted great interest because of their specificity and the duration of action they offer from the standpoint of drug delivery. As used in the present invention, the term "liposome" means a vesicle composed of amphiphilic lipids arranged in a spherical bilayer or bilayers.

[0071] Liposomes are unilamellar or multilamellar vesicles which have a membrane formed from a lipophilic material and an aqueous interior. The aqueous portion contains the composition to be delivered. Cationic liposomes possess the advantage of being able to fuse to the cell wall. Noncationic liposomes, although not able to fuse as efficiently with the cell wall, are taken up by macrophages in vivo.

[0072] In order to cross intact mammalian skin, lipid vesicles must pass through a series of fine pores, each with a diameter less than 50 nm, under the influence of a suitable transdermal gradient. Therefore, it is desirable to use a liposome, which is highly deformable and able to pass through such fine pores.

[0073] Further advantages of liposomes include; liposomes obtained from natural phospholipids are biocompatible and biodegradable; liposomes can incorporate a wide range of water and lipid soluble drugs; liposomes can protect encapsulated drugs in their internal compartments from metabolism and degradation (Rosoff, in *Pharmaceutical Dosage Forms*, Lieberman, Rieger and Banker (Eds.), 1988, Marcel Dekker, Inc., New York, N.Y., volume 1, P. 245). Important considerations in the preparation of liposome formulations are the lipid surface charge, vesicle size, and the aqueous volume of the liposomes.

[0074] Liposomes are useful for the transfer and delivery of active ingredients to the site of action. Because the liposomal membrane is structurally similar to biological membranes, when liposomes are applied to a tissue, the liposomes start to merge with the cellular membranes. As the merging of the liposome and cell progresses, the liposomal contents are emptied into the cell where the active agent may act.

[0075] Liposomal formulations have been the focus of extensive investigation as the mode of delivery for many drugs. There is growing evidence that for topical administration, liposomes present several advantages over other formulations. Such advantages include reduced side-effects related to high systemic absorption of the administered drug, increased accumulation of the administered drug at the desired target, and the ability to administer a wide variety of drugs, both hydrophilic and hydrophobic, into the skin.

[0076] Several reports have detailed the ability of liposomes to deliver agents including high-molecular weight DNA into the skin. Compounds including analgesics, antibodies, hormones, and high-molecular weight DNAs have been administered to the skin. The majority of applications resulted in the targeting of the upper epidermis.

[0077] Liposomes fall into two broad classes. Cationic liposomes are positively charged liposomes, which interact with the negatively charged DNA molecules to form a stable complex. The positively charged DNA/liposome complex binds to the negatively charged cell surface and is internalized in an endosome. Due to the acidic pH within the endosome, the liposomes are ruptured, releasing their contents into the cell cytoplasm (Wang et al., *Biochem. Biophys. Res. Commun.*, 1987, 147, 980 - 985)

[0078] Liposomes, which are pH-sensitive or negatively charged, entrap DNA rather than complex with it. Since both the DNA and the lipid are similarly charged, repulsion rather than complex formation occurs. Nevertheless, some DNA is entrapped within the aqueous interior of these liposomes. pH-sensitive liposomes have been used to deliver DNA encoding the thymidine kinase gene to cell monolayers in culture. Expression of the exogenous gene was detected in the target cells (Zhou et al., *Journal of Controlled Release*, 1992, 19, 269-274).

[0079] One major type of liposomal composition includes phospholipids other than naturally derived phosphatidylcholine. Neutral liposome compositions, for example, can be formed from dimyristoyl phosphatidylcholine (DMPC) or dipalmitoyl phosphatidylcholine (DPPC). Anionic liposome compositions generally are formed from dimyristoyl phosphatidylglycerol, while anionic fusogenic liposomes are formed primarily from dioleoyl phosphatidylethanolamine (DOPE). Another type of liposomal composition is formed from phosphatidylcholine (PC) such as, for example, soybean PC, and egg PC. Another type is formed from mixtures of phospholipid and/or phosphatidylcholine and/or cholesterol.

[0080] Several studies have assessed the topical delivery of liposomal drug formulations to the skin. Application of liposomes containing interferon to guinea pig skin resulted in a reduction of skin herpes sores while delivery of interferon via other means (e.g. as a solution or as an emulsion) were ineffective (Weiner et al., *Journal of Drug Targeting*, 1992, 2, 405-410). Further, an additional study tested the efficacy of interferon administered as part of a liposomal formulation to the administration of interferon using an aqueous system, and concluded that the liposomal formulation was superior to aqueous administration (du Plessis et al., *Antiviral Research*, 1992, 18, 259-265).

[0081] Non-ionic liposomal systems have also been examined to determine their utility in the delivery of drugs to the skin, in particular systems comprising non-ionic surfactant and cholesterol. Non-ionic liposomal formulations comprising Novasome ™ I (glyceryl dilaurate/cholesterol/polyoxyethylene-10-stearyl ether) and Novasome™ II (glyceryl distearate/ cholesterol/polyoxyethylene-10-stearyl ether) were used to deliver cyclosporin-A into the dermis of mouse skin. Results indicated that such non-ionic liposomal systems were effective in facilitating the deposition of cyclosporin-A into different layers of the skin (Hu et al. *S.T.P.Pharma. Sci.*, 1994, 4, 6, 466).

[0082] Liposomes also include "sterically stabilized" liposomes, a term that, as used herein, refers to liposomes comprising one or more specialized lipids that, when incorporated into liposomes, result in enhanced circulation lifetimes relative to liposomes lacking such specialized lipids. Examples of sterically stabilized liposomes are those in which part of the vesicle-forming lipid portion

of the liposome (A) comprises one or more glycolipids, such as monosialoganglioside GM1, or (B) is derivatized with one or more hydrophilic polymers, such as a polyethylene glycol (PEG) moiety. While not wishing to be bound by any particular theory, it is thought in the art that, at least for sterically stabilized liposomes containing gangliosides, sphingomyelin, or PEG-derivatized lipids, the enhanced circulation half-life of these sterically stabilized liposomes derives from a reduced uptake into cells of the reticuloendothelial system (RES) (Allen et al., *FEBS Letters*, 1987, 223, 42; Wu et al., *Cancer Research*, 1993, 53, 3765).

[0083] Various liposomes comprising one or more glycolipids are known in the art. Papahadjopoulos et al. (*Ann. N.Y. Acad. Sci.*, 1987, 507, 64) reported the ability of monosialoganglioside GM1, galactocerebroside sulfate, and phosphatidylinositol to improve blood half-lives of liposomes. These findings were expounded upon by Gabizon et al. (*Proc. Natl. Acad. Sci. U.S.A.*, 1988, 85, 6949), U.S. Patent No. 4,837,028 and WO 88/04924, both to Allen et al., disclose liposomes comprising (1) sphingomyelin and (2) the ganglioside Gjor a galactocerebroside sulfate ester. U.S. Patent No. 5,543,152 (Webb et al.) discloses liposomes comprising sphingomyelin. Liposomes comprising 1,2-sn-dimyristoylphosphatidylcholine are disclosed in WO 97/13499 (Lim et al.).

[0084] Many liposomes comprising lipids derivatized with one or more hydrophilic polymers, and methods of preparation thereof, are known in the art. Sunamoto et al. (*Bull. Chem. Soc. Jpn.*, 1980, 53, 2778) described liposomes comprising a nonionic detergent, 2C1215G, which contains a PEG moiety. Illum et al. (*FEBS Lett.*, 1984, 167, 79) noted that hydrophilic coating of polystyrene particles with polymeric glycols results in significantly enhanced blood half-lives. Synthetic phospholipids modified by the attachment of carboxylic groups of polyalkylene glycols (e.g., PEG) are described by Sears (U.S. Patent Nos. 4,426,330 and 4,534,899). Klibanov et al. (*FEBS Lett.*, 1990, 268, 235) described experiments demonstrating that liposomes comprising phosphatidylethanolamine (PE) derivatized with PEG or PEG stearate have significant increases in blood circulation half-lives. Blume et al. (*Biochimica et Biophysica Acta*, 1990, 1029, 91) extended such observations to other PEG derivatized phospholipids, e.g., DSPE-PEG, formed from the combination of

distearoylphosphatidylethanolamine (DSPE) and PEG. Liposomes having covalently bound PEG moieties on their external surface are described in European Patent No. EP 0 445 131 B1 and WO 90/04384 to Fisher. Liposome compositions containing 1-20 mole percent of PE derivatized with PEG, and methods of use thereof, are described by Woodle et al. (U.S. Patent Nos. 5,013,556 and 5,356,633) and Martin et al. (U.S. Patent No. 5,213,804 and European Patent No. EP 0 496 813 Bl). Liposomes comprising a number of other lipid-polymer conjugates are disclosed in WO 91/05545 and U.S. Patent No. 5,225,212 (both to Martin et al.) and in WO 94/20073 (Zalipsky et al.) Liposomes comprising PEG-modified ceramide lipids are described in WO 96/10391 (Choi et al.). U.S. Patent Nos. 5,540,935 (Miyazaki et al.) and 5,556,948 (Tagawa et al.) describe PEG-containing liposomes that can be further derivatized with functional moieties on their surfaces.

[0085] A limited number of liposomes comprising nucleic acids are known in the art. WO 96/40062 to Thierry et al. discloses methods for encapsulating high molecular weight nucleic acids in liposomes. U.S. Patent No. 5,264,221 to Tagawa et al. discloses protein-bonded liposomes and asserts that the contents of such liposomes may include an antisense RNA. U.S. Patent No. 5,665,710 to Rahman et al. describes certain methods of encapsulating oligodeoxynucleotides in liposomes. WO 97/04787 to Love et al. discloses liposomes comprising antisense oligonucleotides targeted to the raf gene.

[0086] Transfersomes are yet another type of liposomes, and are highly deformable lipid aggregates which are attractive candidates for drug delivery vehicles. Transfersomes may be described as lipid droplets that are so highly deformable that they are easily able to penetrate through pores that are smaller than the droplet. Transfersomes are adaptable to the environment in which they are used, e.g. they are self-optimizing (adaptive to the shape of pores in the skin), self-repairing, frequently reach their targets without fragmenting, and often self-loading. To make transfersomes it is possible to add surface edge-activators, usually surfactants, to a standard liposomal composition. Transfersomes have been used to deliver serum albumin to the skin. The transfersome-mediated delivery of serum albumin has been shown to be as effective as subcutaneous injection of a solution containing serum albumin.

[0087] Surfactants find wide application in formulations such as emulsions (including microemulsions) and liposomes. The most common way of classifying and ranking the properties of the many different types of surfactants, both natural and synthetic, is by the use of the hydrophile/lipophile balance (HLB). The nature of the hydrophilic group (also known as the "head") provides the most useful means for categorizing the different surfactants used in formulations (Rieger, in *Pharmaceutical Dosage Forms*, Marcel Dekker, Inc., New York, NY, 1988, p. 285)

[0088] If the surfactant molecule is not ionized, it is classified as a nonionic surfactant. Nonionic surfactants find wide application in pharmaceutical and cosmetic products and are usable over a wide range of pH values. In general their HLB values range from 2 to about 18 depending on their structure. Nonionic surfactants include nonionic esters such as ethylene glycol esters, propylene glycol esters, glyceryl esters, polyglyceryl esters, sorbitan esters, sucrose esters, and ethoxylated esters. Nonionic alkanolamides and ethers such as fatty alcohol ethoxylates, propoxylated alcohols, and ethoxylated/propoxylated block polymers are also included in this class. The polyoxyethylene surfactants are the most popular members of the nonionic surfactant class.

[0089] If the surfactant molecule carries a negative charge when it is dissolved or dispersed in water, the surfactant is classified as anionic. Anionic surfactants include carboxylates such as soaps, acyl lactylates, acyl amides of amino acids, esters of sulfuric acid such as alkyl sulfates and ethoxylated alkyl sulfates, sulfonates such as alkyl benzene sulfonates, acyl isethionates, acyl taurates and sulfosuccinates, and phosphates. The most important members of the anionic surfactant class are the alkyl sulfates and the soaps.

[0090] If the surfactant molecule carries a positive charge when it is dissolved or dispersed in water, the surfactant is classified as cationic. Cationic surfactants include quaternary ammonium salts and ethoxylated amines. The quaternary ammonium salts are the most used members of this class.

[0091] If the surfactant molecule has the ability to carry either a positive or negative charge, the surfactant is classified as amphoteric. Amphoteric

surfactants include acrylic acid derivatives, substituted alkylamides, N-alkylbetaines, and phosphatides.

[0092] The use of surfactants in drug products, formulations and in emulsions has been reviewed (Rieger, in *Pharmaceutical Dosage Forms*, Marcel Dekker, Inc., New York, NY, 1988, p. 285). Penetration Enhancers

[0093] In one embodiment, the present invention employs various penetration enhancers to effect the efficient delivery of nucleic acids particularly oligonucleotides, to the skin of animals. Most drugs are present in solution in both ionized and nonionized forms. However, usually only lipid soluble or lipophilic drugs readily cross cell membranes. It has been discovered that even non-lipophilic drugs may cross cell membranes if the membrane to be crossed is treated with a penetration enhancer. In addition to aiding the diffusion of non-lipophilic drugs across cell membranes, penetration enhancers also enhance the permeability of lipophilic drugs.

[0094] Penetration enhancers may be classified as belonging to one of five broad categories, i.e., surfactants, fatty acids, bile salts, chelating agents, and non-chelating nonsurfactants (Lee et al., *Critical Reviews in Therapeutic Drug Carrier Systems*, 1991, p.92). Each of the above mentioned classes of penetration enhancers are described below in greater detail.

[0095] Surfactants: In connection with the present invention, surfactants (or "surface-active agents") are chemical entities which, when dissolved in an aqueous solution, reduce the surface tension of the solution or the interfacial tension between the aqueous solution and another liquid, with the result that absorption of oligonucleotides through the mucosa is enhanced. In addition to bile salts and fatty acids, these penetration enhancers include, for example, sodium lauryl sulfate, polyoxyethylene-9-lauryl ether and polyoxyethylene-20-cetyl ether) (Lee et al., *Critical Reviews in Therapeutic Drug Carrier Systems*, 1991, p.92); and perfluorochemical emulsions, such as FC-43. Takahashi et al., *J. Pharm. Pharmacol.*, 1988, 40, 252).

[0096] Fatty acids: Various fatty acids and their derivatives which act as penetration enhancers include, for example, oleic acid, lauric acid, capric acid (n-decanoic acid), myristic acid, palmitic acid, stearic acid, linoleic acid, linolenic acid, dicaprate, tricaprate, monoolein (1-monooleoyl-.rac-glycerol),

dilaurin, caprylic acid, arachidonic acid, glycerol 1-monocaprate, 1-dodecylazacycloheptan-2-one, acylcarnitines, acylcholines, C1-10 alkyl esters thereof (e.g., methyl, isopropyl and t-butyl), and mono- and di-glycerides thereof (i.e., oleate, laurate, caprate, myristate, palmitate, stearate, linoleate, etc.) (Lee et al., *Critical Reviews in Therapeutic Drug Carrier Systems*, 1991, p.92; Muranishi, *Critical Reviews in Therapeutic Drug Carrier Systems*, 1990, 7, 1-33; El Hariri et al., *J. Pharm. Pharmacol.*, 1992, 44, 651-654).

[0097] Bile salts: The physiological role of bile includes the facilitation of dispersion and absorption of lipids and fat-soluble vitamins (Brunton, Chapter 38 in: Goodman & Gilman's *The Pharmacological Basis of Therapeutics*, 9th Ed., Hardman et al. Eds. McGraw-Hill, New York, 1996, pp. 934-935). Various natural bile salts, and their synthetic derivatives, act as penetration enhancers. Thus the term "bile salts" includes any of the naturally occurring components of bile as well as any of their synthetic derivatives. The bile salts of the invention include, for example, cholic acid (or its pharmaceutically acceptable sodium salt, sodium cholate), dehydrocholic acid (sodium dehydrocholate), deoxycholic acid (sodium deoxycholate), glucholic acid (sodium glucholate), glycholic acid (sodium glycocholate), glycodeoxycholic acid (sodium glycodeoxycholate), taurocholic acid (sodium taurocholate), taurodeoxycholic acid (sodium taurodeoxycholate), chenodeoxycholic acid (sodium chenodeoxycholate), ursodeoxycholic acid (UDCA), sodium tauro-24,25-dihydro-fusidate (STDHF), sodium glycodihydrofusidate and polyoxyethylene-9-lauryl ether (POE) (Lee et al., *Critical Reviews in Therapeutic Drug Carrier Systems*, 1991, page 92; Swinyard, Chapter 39 In: *Remington's Pharmaceutical Sciences*, 18th Ed., Gennaro, ed., Mack Publishing Co., Easton, PA, 1990, pages 782-783; Muranishi, *Critical Reviews in Therapeutic Drug Carrier Systems*, 1990, 7, 1-33; Yamamoto et al., *J. Pharm. Exp. Ther.*, 1992, 263, 25; Yamashita et al., *J. Pharm. Sci.*, 1990, 79, 579-583).

[0098] Chelating Agents: Chelating agents, as used in connection with the present invention, can be defined as compounds that remove metallic ions from solution by forming complexes therewith, with the result that absorption of oligonucleotides through the mucosa is enhanced. With regards to their use as penetration enhancers in the present invention, chelating agents have the added

advantage of also serving as DNase inhibitors, as most characterized DNA nucleases require a divalent metal ion for catalysis and are thus inhibited by chelating agents (Jarrett, *J. Chromatogr.*, 1993, 618, 315-339). Chelating agents of the invention include but are not limited to disodium ethylenediaminetetraacetate (EDTA), citric acid, salicylates (e.g., sodium salicylate, 5-methoxysalicylate and homovanilate), N-acyl derivatives of collagen, laureth-9 and N-amino acyl derivatives of beta-diketones (enamines)(Lee et al., *Critical Reviews in Therapeutic Drug Carrier Systems*, 1991, page 92; Muranishi, *Critical Reviews in Therapeutic Drug Carrier Systems*, 1990, 7, 1-33; Buur et al., *J. Control Rel.*, 1990, 14, 43-51).

[0099] Non-chelating non-surfactants: As used herein, nonchelating non-surfactant penetration enhancing compounds can be defined as compounds that demonstrate insignificant activity as chelating agents or as surfactants but that nonetheless enhance absorption of oligonucleotides through the alimentary mucosa (Muranishi, *Critical Reviews in Therapeutic Drug Carrier Systems*, 1990, 7, 1-33). This class of penetration enhancers includes, for example, unsaturated cyclic ureas, 1-alkyl- and 1-alkenylazacyclo-alkanone derivatives (Lee et al., *Critical Reviews in Therapeutic Drug Carrier Systems*, 1991, page 92); and non-steroidal anti-inflammatory agents such as diclofenac sodium, indomethacin, and phenylbutazone (Yamashita et al., *J. Pharm. Pharmacol.*, 1987, 39, 621-626).

[00100] Agents that enhance uptake of oligonucleotides at the cellular level may also be added to the pharmaceutical and other compositions of the present invention. For example, cationic lipids, such as lipofectin (Junichi et al, U.S. Patent No. 5,705,188), cationic glycerol derivatives, and polycationic molecules, such as polylysine (Lollo et al., PCT Application WO 97/30731), are also known to enhance the cellular uptake of oligonucleotides.

[00101] Other agents may be utilized to enhance the penetration of the administered nucleic acids, including glycols such as ethylene glycol and propylene glycol, pyrrols such as 2-pyrrol, azones, and terpenes such as limonene and menthone.

Carriers

[00102] Certain compositions of the present invention also incorporate carrier compounds in the formulation. As used herein, "carrier compound" or "carrier" can refer to a nucleic acid, or analog thereof, which is inert (i.e., does not possess biological activity per se) but is recognized as a nucleic acid by in vivo processes that reduce the bioavailability of a nucleic acid having biological activity by, for example, degrading the biologically active nucleic acid or promoting its removal from circulation. The coadministration of a nucleic acid and a carrier compound, typically with an excess of the latter substance, can result in a substantial reduction of the amount of nucleic acid recovered in the liver, kidney or other extracirculatory reservoirs, presumably due to competition between the carrier compound and the nucleic acid for a common receptor. For example, the recovery of a partially phosphorothioate oligonucleotide in hepatic tissue can be reduced when it is coadministered with polyinosinic acid, dextran sulfate, polycytidic acid or 4-acetamido-4'isothiocyano-stilbene-2,2'disulfonic acid (Miyao et al., *Antisense Res. Dev.*, 1995, 5, 115-121; Takakura et al., *Antisense & Nucl. Acid Drug Dev.*, 1996, 6, 177-183).

Excipients

[00103] In contrast to a carrier compound, a "pharmaceutical carrier" or "excipient" is a pharmaceutically acceptable solvent, suspending agent or any other pharmacologically inert vehicle for delivering one or more nucleic acids to an animal. The excipient may be liquid or solid and is selected, with the planned manner of administration in mind, so as to provide for the desired bulk, consistency, etc., when combined with a nucleic acid and the other components of a given pharmaceutical composition. Typical pharmaceutical carriers include, but are not limited to, binding agents (e.g., pregelatinized maize starch, polyvinylpyrrolidone or hydroxypropyl methylcellulose, etc.); fillers (e.g., lactose and other sugars, microcrystalline cellulose, pectin, gelatin, calcium sulfate, ethyl cellulose, polyacrylates or calcium hydrogen phosphate, etc.); lubricants (e.g., magnesium stearate, talc, silica, colloidal silicon dioxide, stearic acid, metallic stearates, hydrogenated vegetable oils, corn starch, polyethylene glycols, sodium benzoate, sodium acetate, etc.); disintegrants (e.g., starch,

sodium starch glycolate, etc.); and wetting agents (e.g., sodium lauryl sulphate, etc.).

[00104] Pharmaceutically acceptable organic or inorganic excipient suitable for non-parenteral administration, which does not deleteriously react with nucleic acids, can also be used to formulate the compositions of the present invention. Suitable pharmaceutically acceptable carriers include, but are not limited to, water, salt solutions, alcohols, polyethylene glycols, gelatin, lactose, amylose, magnesium stearate, talc, silicic acid, viscous paraffin, hydroxymethylcellulose, polyvinylpyrrolidone and the like.

[00105] Formulations for topical administration of nucleic acids may include sterile and non-sterile aqueous solutions, non-aqueous solutions in common solvents such as alcohols, or solutions of the nucleic acids in liquid or solid oil bases. The solutions may also contain buffers, diluents, and other suitable additives. Pharmaceutically acceptable organic or inorganic excipients suitable for non-parenteral administration that do not deleteriously react with nucleic acids can be used.

[00106] Suitable pharmaceutically acceptable excipients include, but are not limited to, water, salt solutions, alcohol, polyethylene glycols, gelatin, lactose, amylose, magnesium stearate, talc, silicic acid, viscous paraffin, hydroxymethylcellulose, polyvinylpyrrolidone and the like.

Other Components

[00107] The compositions of the present invention may additionally contain other adjunct components conventionally found in pharmaceutical compositions, at their art-established usage levels. Thus, for example, the compositions may contain additional, compatible, pharmaceutically-active materials such as, for example, antipruritics, astringents, local anesthetics or anti-inflammatory agents, or may contain additional materials useful in physically formulating various dosage forms of the compositions of the present invention, such as dyes, flavoring agents, preservatives, antioxidants, opacifiers, thickening agents and stabilizers. However, such materials, when added, should not unduly interfere with the biological activities of the components of the compositions of the present invention. The formulations can be sterilized and, if

desired, mixed with auxiliary agents, e.g., lubricants, preservatives, stabilizers, wetting agents, emulsifiers, salts for influencing osmotic pressure, buffers, colorings, flavorings and/or aromatic substances and the like which do not deleteriously interact with the nucleic acid(s) of the formulation.

[00108] Aqueous suspensions may contain substances that increase the viscosity of the suspension including, for example, sodium carboxymethylcellulose, sorbitol, and/or dextran. The suspension may also contain stabilizers.

[00109] Certain embodiments of the invention provide pharmaceutical compositions containing (a) one or more antisense compounds and (b) one or more other chemotherapeutic agents which function by a non-antisense mechanism. Examples of such chemotherapeutic agents include, but are not limited to, anticancer drugs such as daunorubicin, dactinomycin, doxorubicin, bleomycin, mitomycin, nitrogen mustard, chlorambucil, melphalan, cyclophosphamide, 6-mercaptopurine, 6-thioguanine, cytarabine (CA), 5-fluorouracil (5-FU), floxuridine (5-FUdR), methotrexate (MTX), colchicine, vincristine, vinblastine, etoposide, teniposide, cisplatin and diethylstilbestrol (DES). See, generally, *The Merck Manual of Diagnosis and Therapy*, 15th Ed., Berkow et al., eds., 1987, Rahway, N.J., pages 1206-1228). Anti-inflammatory drugs, including but not limited to nonsteroidal anti-inflammatory drugs and corticosteroids, and antiviral drugs, including but not limited to ribivirin, vidarabine, acyclovir and ganciclovir, may also be combined in compositions of the invention. See, generally, *The Merck Manual of Diagnosis and Therapy*, 15th Ed., Berkow et al., eds., 1987, Rahway, N.J., pages 2499-2506 and 46-49, respectively) other non-antisense chemotherapeutic agents are also within the scope of this invention. Two or more combined compounds may be used together or sequentially.

[00110] In another related embodiment, compositions of the invention may contain one or more antisense compounds, particularly oligonucleotides, targeted to a first nucleic acid and one or more additional antisense compounds targeted to a second nucleic acid target. Numerous examples of antisense compounds are known in the art. Two or more combined compounds may be used together or sequentially.

[00111] The formulation of therapeutic compositions and their subsequent administration is believed to be within the skill of those in the art. Dosing is dependent on severity and responsiveness of the disease state to be treated, with the course of treatment lasting from several days to several months, or until a cure is effected or a diminution of the disease state is achieved. Optimal dosing schedules can be calculated from measurements of drug accumulation in the body of the patient. Persons of ordinary skill can easily determine optimum dosages, dosing methodologies and repetition rates. Optimum dosages may vary depending on the relative potency of individual oligonucleotides, and can generally be estimated based on EC50s found to be effective in in vitro and in vivo animal models. In general, dosage is from 0.01 μg to 100 g per kg of body weight, and may be given once or more daily, weekly, monthly or yearly, or even once every 2 to 20 years. Persons of ordinary skill in the art can easily estimate repetition rates for dosing based on measured residence times and concentrations of the drug in bodily fluids or tissues. Following successful treatment, it may be desirable to have the patient undergo maintenance therapy to prevent the recurrence of the disease state, wherein the oligonucleotide is administered in maintenance doses, ranging from 0.01 μg to 100 g per kg of body weight, once or more daily, to once every 20 years.

[00112] While the present invention has been described with specificity in accordance with certain of its preferred embodiments, the following examples serve only to illustrate the invention and are not intended to limit the same.

EXAMPLES

Example 1

Nucleoside Phosphoramidites for Oligonucleotide Synthesis Deoxy and 2'-alkoxy amidites

[00113] 2'-Deoxy and 2'-methoxy beta-cyanoethyldiisopropyl phosphoramidites are available from commercial sources (e.g. Chemgenes, Needham MA or Glen Research, Inc. Sterling VA). Other 2'-O-alkoxy substituted nucleoside amidites are prepared as described in U.S. Patent

5,506,351, herein incorporated by reference. For oligonucleotides synthesized using 2'-alkoxy amidites, the standard cycle for unmodified oligonucleotides is utilized, except the wait step after pulse delivery of tetrazole and base is increased to 360 seconds.

[00114] Oligonucleotides containing 5-methyl-2'-deoxycytidine (5-Me-C) nucleotides are synthesized according to published methods [Sanghvi, et. al., *Nucleic Acids Research*, 1993, 21, 3197-3203] using commercially available phosphoramidites (Glen Research, Sterling VA or ChemGenes, Needham MA).

2'-Fluoro amidites

2'-Fluorodeoxyadenosine amidites

[00115] 2'-fluoro oligonucleotides are synthesized as described previously [Kawasaki, et. al., *J. Med. Chem.*, 1993, 36, 831-841] and United States patent 5,670,633, herein incorporated by reference. Briefly, the protected nucleoside N6-benzoyl-2'-deoxy-2'-fluoroadenosine is synthesized utilizing commercially available 9-beta-D-arabinofuranosyladenine as starting material and by modifying literature procedures whereby the 2'-alpha-fluoro atom is introduced by an S_N2-displacement of a 2'-beta-trityl group. Thus N6-benzoyl-9-beta-D-arabinofuranosyladenine is selectively protected in moderate yield as the 3', 5'-ditetrahydropyranyl (THP) intermediate. Deprotection of the THP and N6-benzoyl groups is accomplished using standard methodologies and standard methods are used to obtain the 5'-dimethoxytrityl-(DMT) and 5'-DMT-3'-phosphoramidite intermediates.

2'-Fluorodeoxyguanosine

[00116] The synthesis of 2'-deoxy-2'-fluoroguanosine is accomplished using tetraisopropyldisiloxanyl (TPDS) protected 9-beta-D-arabinofuranosylguanine as starting material, and conversion to the intermediate diisobutyrylarabinofuranosylguanosine. Deprotection of the TPDS group is followed by protection of the hydroxyl group with THP to give diisobutyryl di-THP protected arabinofuranosylguanine. Selective O-deacylation and triflation is followed by treatment of the crude product with fluoride, then deprotection of

the THP groups. Standard methodologies are used to obtain the 5'-DMT- and 5'-DMT-3'-phosphoramidites.

2'-Fluorouridine

[00117] Synthesis of 2'-deoxy-2'-fluorouridine is accomplished by the modification of a literature procedure in which 2,2'anhydro-l-beta-D-arabinofuranosyluracil is treated with 70% hydrogen fluoride-pyridine. Standard procedures are used to obtain the 5'-DMT and 5'-DMT-3'-phosphoramidites.

2'-Fluorodeoxycytidine

[00118] 2'-deoxy-2'-fluorocytidine is synthesized via amination of 2'-deoxy-2'-fluorouridine, followed by selective protection to give N4-benzoyl-2'-deoxy-2'-fluorocytidine. Standard procedures are used to obtain the 5'-DMT and 5'-DMT-3'phosphoramidites.

2'-O-(2-Methoxyethyl) modified amidites

[00119] 2'-O-Methoxyethyl-substituted nucleoside amidites are prepared as follows, or alternatively, as per the methods of Martin, P., *Helvetica Chimica Acta*, 1995, 78, 486-504.

2,2'-Anhydro[l-(beta-D-arabinofuranosyl)-5-methyluridinel

[00120] 5-Methyluridine (ribosylthymine, commercially available through Yamasa, Choshi, Japan) (72.0 g, 0.279 M), diphenylcarbonate (90.0 g, 0.420 M) and sodium bicarbonate (2.0 g, 0.024 M) are added to DMF (300 mL). The mixture is heated to reflux, with stirring, allowing the evolved carbon dioxide gas to be released in a controlled manner. After 1 hour, the slightly darkened solution is concentrated under reduced pressure. The resulting syrup is poured into diethylether (2.5 L), with stirring. The product formed a gum. The ether is decanted and the residue is dissolved in a minimum amount of methanol (ca. 400 mL). The solution is poured into fresh ether (2.5 L) to yield a stiff gum. The ether is decanted and the gum is dried in a vacuum oven (60°C at 1 mm Hg for 24 h) to give a solid that is crushed to a light tan powder. The material is used as

is for further reactions (or it can be purified further by column chromatography using a gradient of methanol in ethyl acetate (10-25%) to give a white solid.

2'-O-Methoxyethyl-5-methyluridine

[00121] 2,2'-Anhydro-5-methyluridine (195 g, 0.81 M), tris(2-methoxyethyl)borate (231 g, 0.98 M) and 2-methoxyethanol (1.2 L) are added to a 2 L stainless steel pressure vessel and placed in a pre-heated oil bath at 160°C. After heating for 48 hours at 155-160°C, the vessel is opened and the solution evaporated to dryness and triturated with MeOH (200 mL). The residue is suspended in hot acetone (1 L). The insoluble salts are filtered, washed with acetone (150 mL) and the filtrate evaporated. The residue (280 g) is dissolved in CH_3CN (600 mL) and evaporated. A silica gel column (3 kg) is packed in CH_2Cl_2 /acetone /MeOH (20:5:3) containing 0.5% Et_3NH. The residue is dissolved in CH_2Cl_2 (250 mL) and adsorbed onto silica (150 g) prior to loading onto the column. The product is eluted with the packing solvent to give the title product. Additional material can be obtained by reworking impure fractions.

2'-O-Methoxyethyl-5'-O-dimethoxytrityl-5-methyluridine

[00122] 2'-O-Methoxyethyl-5-methyluridine (160 g, 0.506 M) is co-evaporated with pyridine (250 mL) and the dried residue dissolved in pyridine (1.3 L). A first aliquot of dimethoxytrityl chloride (94.3 g, 0.278 M) is added and the mixture stirred at room temperature for one hour. A second aliquot of dimethoxytrityl chloride (94.3 g, 0.278 M) is added and the reaction stirred for an additional one hour. Methanol (170 mL) is then added to stop the reaction. The solvent is evaporated and triturated with CH_3CN (200 mL) The residue is dissolved in CHCl (1.5 L) and extracted with 2x500 mL of saturated $NaHCO_3$ and 2x500 mL of saturated NaCl. The organic phase is dried over Na_2SO_4, filtered, and evaporated. The residue is purified on a 3.5 kg silica gel column, packed and eluted with EtOAc/hexane/ acetone (5:5:1) containing 0-5% Et_3NH. The pure fractions are evaporated to give the title product.

3'-O-Acetyl-2'-O-methoxyethyl-5'-O-dimethoxytrityl-5-methyluridine

[00123] 2'-O-Methoxyethyl-5'-O-dimethoxytrityl-5-methyluridine (106 g, 0.167 M), DMF/pyridine (750 mL of a 3:1 mixture prepared from 562 mL of DMF and 188 mL of pyridine) and acetic anhydride (24.38 mL, 0.258 M) are combined and stirred at room temperature for 24 hours. The reaction is monitored by TLC by first quenching the TLC sample with the addition of MeOH. Upon completion of the reaction, as judged by TLC, MeOH (50 mL) is added and the mixture evaporated at 35°C. The residue is dissolved in $CHCl_3$ (800 mL) and extracted with 2x200 mL of saturated sodium bicarbonate and 2x200 mL of saturated NaCl. The water layers are back extracted with 200 mL of $CHCl_3$. The combined organics are dried with sodium sulfate and evaporated to a residue. The residue is purified on a 3.5 kg silica gel column and eluted using EtOAc/hexane(4:1). Pure product fractions are evaporated to yield the title compounds.

3'-O-Acetyl-2'-O-methoxyethyl-5'-O-dimethoxytrityl-5-methyl-4-triazoleuridine

[00124] A first solution is prepared by dissolving 3'-O-acetyl-2'-O-methoxyethyl-5'-O-dimethoxytrityl-5-methyluridine (96 g, 0.144 M) in CH_3CN (700 mL) and set aside. Triethylamine (189 mL, 1.44 M) is added to a solution of triazole (90 g, 1.3 M) in CH_3CN (1 L), cooled to –5°C and stirred for 0.5 h using an overhead stirrer. $POCl_3$ is added dropwise, over a 30 minute period, to the stirred solution maintained at 0-10°C, and the resulting mixture stirred for an additional 2 hours. The first solution is added dropwise, over a 45 minute period, to the latter solution. The resulting reaction mixture is stored overnight in a cold room. Salts are filtered from the reaction mixture and the solution is evaporated. The residue is dissolved in EtOAc (1 L) and the insoluble solids are removed by filtration. The filtrate is washed with 1x300 mL of $NaHCO_3$ and 2x300 mL of saturated NaCl, dried over sodium sulfate and evaporated. The residue is triturated with EtOAc to give the title compound.

2'-O-Methoxyethyl-5'-O-dimethoxytrityl-5-methylcytidine

[00125] A solution of 3'-O-acetyl-2'-O-methoxyethyl-5'-O-dimethoxytrityl-5-methyl-4-triazoleuridine (103 g, 0.141 M) in dioxane (500 mL) and NH_4OH (30 mL) is stirred at room temperature for 2 hours. The dioxane solution is evaporated and the residue azeotroped with MeOH (2x200 mL). The residue is dissolved in MeOH (300 mL) and transferred to a 2-liter stainless steel pressure vessel. MeOH (400 mL) saturated with NH_3 gas is added and the vessel heated to 100°C for 2 hours (TLC showed complete conversion). The vessel contents are evaporated to dryness and the residue is dissolved in EtOAc (500 mL) and washed once with saturated NaCl (200 mL). The organics are dried over sodium sulfate and the solvent is evaporated to give the title compound.

N4-Benzoyl-2'-O-methoxyethyl-5'-O-dimethoxytrityl-5-methylcytidine

[00126] 2'-O-Methoxyethyl-5'-O-dimethoxytrityl-5-methylcytidine (85 g, 0.134 M) is dissolved in DMF (800 mL) and benzoic anhydride (37.2 g, 0.165 M) is added with stirring. After stirring for 3 hours, TLC showed the reaction to be approximately 95% complete. The solvent is evaporated and the residue azeotroped with MeOH (200 mL). The residue is dissolved in $CHC1_3$ (700 mL) and extracted with saturated NaHCO, (2x300 mL) and saturated NaCl (2x300 mL), dried over $MgSO_4$ and evaporated to give a residue. The residue is chromatographed on a 1.5 kg silica column using EtOAc/hexane (1:1) containing 0-5% Et_3NH as the eluting solvent. The pure product fractions are evaporated to give the title compound.

N4-Benzoyl-2'-O-methoxyethyl-5'-O-dimethoxytrityl-5-methylcytidine-3'-amidite

[00127] N4-Benzoyl-2'-O-methoxyethyl-5'-O-dimethoxytrityl-5-methylcytidine (74 g, 0.10 M) is dissolved in CH_2Cl_2 (1 L) Tetrazole diisopropylamine (7.1 g) and 2-cyanoethoxy-tetra(isopropyl)phosphite (40.5 mL, 0.123 M) are added with stirring, under a nitrogen atmosphere. The resulting mixture is stirred for 20 hours at room temperature (TLC showed the reaction to be 95% complete). The reaction mixture is extracted with saturated $NaHCO_3$ (1x300 mL) and saturated NaCl (3x300 mL). The aqueous washes are

back-extracted with CH_2Cl_2 (300 mL), and the extracts are combined, dried over $MgSO_4$, and concentrated. The residue obtained is chromatographed on a 1.5 kg silica column using EtOAc/hexane (3:1) as the eluting solvent. The pure fractions were combined to give the title compound.

2'-O-(Aminooxyethyl) nucleoside amidites and 2'-O-(dimethylaminooxyethyl) nucleoside amidites

2'-(Dimethylaminooxyethoxy) nucleoside amidites

[00128] 2'-(Dimethylaminooxyethoxy) nucleoside amidites [also known in the art as 2'-O-(dimethylaminooxyethyl) nucleoside amidites] are prepared as described in the following paragraphs. Adenosine, cytidine and guanosine nucleoside amidites are prepared similarly to the thymidine (5-methyluridine) except the exocyclic amines are protected with a benzoyl moiety in the case of adenosine and cytidine and with isobutyryl in the case of guanosine.

5'-O-tert-Butyldiphenylsilyl -O^2 -2'-anhydro-5-methyluridine

[00129] O^2 -2'-anhydro-5-methyluridine (Pro. Bio. Sint., Varese, Italy, 100.0g, 0.4'6 mmol), dimethylaminopyridine (0.66g, 0.013eq, 0.0054mmol) are dissolved in dry pyridine (500 ml) at ambient temperature under an argon atmosphere and with mechanical stirring tert-Butyldiphenylchlorosilane (125.8g, 119.0mL, 1.1eq, 0.458mmol) is added in one portion. The reaction is stirred for 16 h at ambient temperature. TLC (Rf 0.22, ethyl acetate) indicated a complete reaction. The solution is concentrated under reduced pressure to a thick oil. This is partitioned between dichloromethane (1 L) and saturated sodium bicarbonate (2xl L) and brine (1 L). The organic layer is dried over sodium sulfate and concentrated under reduced pressure to a thick oil. The oil is dissolved in a 1:1 mixture of ethyl acetate and ethyl ether (600mL) and the solution is cooled to –10°C. The resulting crystalline product is collected by filtration, washed with ethyl ether (3x200 mL), and dried (40°C, 1mm Hg, 24 h) to a white solid.

5'-O-tert-Butyldiphenylsilyl-2'-O-(2-hydroxyethyl)-5-methyluridine

[00130] In a 2 L stainless steel, unstirred pressure reactor is added borane in tetrahydrofuran (1.0 M, 2.0 eq, 622 mL). In the fume hood and with manual stirring, ethylene glycol (350 mL, excess) is added cautiously at first until the evolution of hydrogen gas subsides. 5'-O-tert-Butyldiphenylsilyl-O^2-2'anhydro-5-methyluridine (149 g, 0.3'1 mol) and sodium bicarbonate (0.074 g, 0.003 eq) are added with manual stirring. The reactor is sealed and heated in an oil bath until an internal temperature of 160°C is reached and then maintained for 16 h (pressure < 100 psig). The reaction vessel is cooled to ambient and opened. TLC (Rf 0.67 for desired product and Rf 0.82 for ara-T side product, ethyl acetate) indicated about 70% conversion to the product. In order to avoid additional side product formation, the reaction is stopped, concentrated under reduced pressure (10 to 1mm, Hg) in a warm water bath (40-100°C) with the more extreme conditions used to remove the ethylene glycol. [Alternatively, once the low boiling solvent is gone, the remaining solution can be partitioned between ethyl acetate and water. The product will be in the organic phase.] The residue is purified by column chromatography (2kg silica gel, ethyl acetate-hexanes gradient 1:1 to 4:1). The appropriate fractions are combined, stripped, and dried to product as a white crisp foam, contaminated starting material, and pure reusable starting material.

2'-O-([2-phthalimidoxy)ethyl]-5'-t-butyldiphenylsilyl-5-methyluridine

[00131] 5'-O-tert-Butyldiphenylsilyl-2'-O-(2-hydroxyethyl)-5- methyluridine (20g, 36.98mmol) is mixed with triphenylphosphine (11.63g, 44.36mmol) and N-hydroxyphthalimide (7.24g, 44.36mmol). It is then dried over P_2O_5 under high vacuum for two days at 40°C. The reaction mixture is flushed with argon and dry THF (369.8mL, Aldrich, sure seal bottle) is added to get a clear solution. Diethyl-azodicarboxylate (6.98mL, 44.36mmol) is added dropwise to the reaction mixture. The rate of addition is maintained such that resulting deep red coloration is just discharged before adding the next drop. After the addition is complete, the reaction is stirred for 4 hrs. By that time TLC showed the completion of the reaction (ethylacetate:hexane, 60:40). The solvent is evaporated in vacuum. Residue obtained is placed on a flash column and eluted

with ethyl acetate:hexane (60:40), to get 2'-O-([2-phthalimidoxy)ethyl]-5'-t-butyldiphenylsilyl-5-methyluridine as white foam.

5'-O-tert-butyldiphenylsilyl-2'-O-[(2-formadoximinooxy)ethyl]-5-methyluridine

[00132] 2'-O-([2-phthalimidoxy)ethyl]-5'-t-butyldiphenylsilyl-5-methyluridine (3.1g, 4.5mmol) is dissolved in dry CH_2Cl_2 (4.5mL) and methylhydrazine (300mL, 4.64mmol) is added dropwise at –10°C to 0°C. After 1 h the mixture is filtered, the filtrate is washed with ice cold CH_2Cl_2 and the combined organic phase is washed with water, brine and dried over anhydrous Na_2SO_4. The solution is concentrated to get 2'-O(aminooxyethyl) thymidine, which is then dissolved in MeOH (67.5mL). To this formaldehyde (20% aqueous solution, w/w, 1.1 eq.) is added and the resulting mixture is stirred for 1 h. Solvent is removed under vacuum; residue chromatographed to get 5'-O-tert-butyldiphenylsilyl-2'-O-[(2-formadoximinooxy) ethyl]-5-methyluridine as white foam.

5'-O-tert-Butyldiphenylsilyl-2'-O-[N,N-dimethylaminooxyethyl]-5-methyluridine

[00133] 5'-O-tert-butyldiphenylsilyl-2'-O-[(2- formadoximinooxy)ethyl]-5-methyluridine (1.77g, 3.12mmol) is dissolved in a solution of 1M pyridinium p-toluenesulfonate (PPTS) in dry MeOH (30.6mL). Sodium cyanoborohydride (0.39g, 6.13mmol) is added to this solution at 10°C under inert atmosphere. The reaction mixture is stirred for 10 minutes at 10°C. After that the reaction vessel is removed from the ice bath and stirred at room temperature for 2 h, the reaction monitored by TLC (5% MeOH in CH_2Cl_2). Aqueous $NaHCO_3$ solution (5%, 10mL) is added and extracted with ethyl acetate (2x20mL). Ethyl acetate phase is dried over anhydrous Na_2SO_4, evaporated to dryness. Residue is dissolved in a solution of 1M PPTS in MeOH (30.6mL). Formaldehyde (20% w/w, 30mL, 3.37mmol) is added and the reaction mixture is stirred at room temperature for 10 minutes. Reaction mixture cooled to 10°C in an ice bath, sodium cyanoborohydride (0.39g, 6.13mmol) is added, and reaction mixture stirred at 10°C for 10 minutes. After 10 minutes, the reaction mixture is

removed from the ice bath and stirred at room temperature for 2 hrs. To the reaction mixture 5% $NaHCO_3$ (25mL) solution is added and extracted with ethyl acetate (2x25mL). Ethyl acetate layer is dried over anhydrous Na_2SO_4 and evaporated to dryness. The residue obtained is purified by flash column chromatography and eluted with 5% MeOH in CH_2Cl_2 to get 5'-O-tertbutyldiphenylsilyl-2'-O-[N,N-dimethylaminooxyethyl]-5- methyluridine as a white foam.

2'-O-(dimethylaminooxyethyl)-5-methyluridine

[00134] Triethylamine trihydrofluoride (3.91mL, 24.0mmol) is dissolved in dry THF and triethylamine (1.67mL, 12mmol, dry, kept over KOH). This mixture of triethylamine-2HF is then added to 5'-O-tert-butyldiphenylsilyl-2'-O-[N,N-dimethylaminooxyethyl]-5-methyluridine (1.40g, 2.4mmol) and stirred at room temperature for 24 hrs. Reaction is monitored by TLC (5% MeOH in CH_2Cl_2). Solvent is removed under vacuum and the residue placed on a flash column and eluted with 10% MeOH in CH_2Cl_2 to get 2'-O-(dimethylaminooxyethyl)-5-methyluridine.

5'-O-DMT-2'-O-(dimethylaminooxyethyl)-5-methyluridine

[00135] 2'-O-(dimethylaminooxyethyl)-5-methyluridine (750mg, 2.17mmol) is dried over P_2O_5 under high vacuum overnight at 40°C. It is then co-evaporated with anhydrous pyridine (20mL). The residue obtained is dissolved in pyridine (11mL) under argon atmosphere. 4-dimethylaminopyridine (26.5mg, 2.60mmol), 4,4'-dimethoxytrityl chloride (880mg, 2.60mmol) is added to the mixture and the reaction mixture is stirred at room temperature until all of the starting material disappeared. Pyridine is removed under vacuum and the residue chromatographed and eluted with 10% MeOH in CH_2Cl_2 (containing a few drops of pyridine) to get 5'-O-DMT-2'-0(dimethylamino-oxyethyl)-5-methyluridine.

5'-O-DMT-2'-O-(2-N,N-dimethylaminooxyethyl)-5-methyluridine-3'-[(2-cyanoethyl)-N,N- diisopropylphosphoramidite]

[00136] 5'-O-DMT-2'-O-(dimethylaminooxyethyl)-5-methyluridine (1.08g, 1.67mmol) is co-evaporated with toluene (20mL). To the residue N,N-diisopropylamine tetrazonide (0.29g, 1.67mmol) is added and dried over P20, under high vacuum overnight at 40°C. Then the reaction mixture is dissolved in anhydrous acetonitrile (8.4mL) and 2-cyanoethyl-N,N,N^1,N^1-tetraisopropylphosphoramidite (2.12mL, 6.08mmol) is added. The reaction mixture is stirred at ambient temperature for 4 hrs under inert atmosphere. The progress of the reaction is monitored by TLC (hexane:ethyl acetate 1:1). The solvent is evaporated, then the residue is dissolved in ethyl acetate (70mL) and washed with 5% aqueous $NaHCO_3$ (40mL). Ethyl acetate layer is dried over anhydrous Na_2SO_4 and concentrated. Residue obtained is chromatographed (ethyl acetate as eluent) to get 5'-O-DMT-2'-O-(2-N,N-dimethylaminooxyethyl)-5-methyluridine-3'-[(2-cyanoethyl)-N,N-diisopropylphosphoramidite] as a foam.

2'-(Aminooxyethoxy) nucleoside amidites

[00137] 2'-(Aminooxyethoxy) nucleoside amidites [also known in the art as 2'-O-(aminooxyethyl) nucleoside amidites] are prepared as described in the following paragraphs. Adenosine, cytidine and thymidine nucleoside amidites are prepared similarly.

N2-isobutyryl-6-O-diphenylcarbamoyl-2'-O-(2-ethylacetyl)-5'-O-(4,4'-dimethoxytrityl)guanosine-3'-[(2-cyanoethyl)-N,N-diisopropylphosphoramidite]

[00138] The 2'-O-aminooxyethyl guanosine analog may be obtained by selective 2'-O-alkylation of diaminopurine riboside. Multigram quantities of diaminopurine riboside may be purchased from Schering AG (Berlin) to provide 2'-O-(2-ethylacetyl) diaminopurine riboside along with a minor amount of the 3'-O-isomer. 2'-O-(2-ethylacetyl) diaminopurine riboside may be resolved and converted to 2'-O-(2ethylacetyl)guanosine by treatment with adenosine deaminase. (McGee, D. P. C., Cook, P. D., Guinosso, C. J., WO 94/02501 Al

940203.) Standard protection procedures should afford 2'-O-(2-ethylacetyl)-5'-O-(4,4'-dimethoxytrityl)guanosine and 2-N-isobutyryl-6-O-diphenylcarbamoyl-2'-O-(2-ethylacetyl)-5'-O-(4,4'-dimethoxytrityl)guanosine which may be reduced to provide 2-N-isobutyryl-6-O-diphenylcarbamoyl-2'-O-(2-ethylacetyl)-5'-O-(4,4'-dimethoxytrityl)guanosine. As before the hydroxyl group may be displaced by N-hydroxyphthalimide via a Mitsunobu reaction, and the protected nucleoside may phosphitylated as usual to yield 2-N-isobutyryl-6-O-diphenylcarbamoyl-2'-O-(2-ethylacetyl)-5'-O-(4,4'-dimethoxytrityl)guanosine-3'-[(2-cyanoethyl)-N,N-diisopropylphosphoramiditel.

2'-dimethylaminoethoxyethoxy (2'-DMAEOE) nucleoside amidites

[00139] 2'-dimethylaminoethoxyethoxy nucleoside amidites (also known in the art as 2'-O-dimethylaminoethoxyethyl, i.e., 2'O-CH_2-O-CH_2-N$(CH_2)_2$, or 2'-DMAEOE nucleoside amidites) are prepared as follows. Other nucleoside amidites are prepared similarly.

2'-O-[2(2-N,N-dimethylaminoethoxy)ethyl]-5-methyl uridine

[00140] 2[2-(Dimethylamino)ethoxylethanol (Aldrich, 6.66 g, 50 mmol) is slowly added to a solution of borane in tetrahydrofuran (1 M, 10 mL, 10 mmol) with stirring in a 100 mL bomb. Hydrogen gas evolves as the solid dissolves. O^2-, 2' - anhydro-5-methyluridine (1.2 g, 5 mmol), and sodium bicarbonate (2.5 mg) are added and the bomb is sealed, placed in an oil bath, and heated to 155°C for 26 hours. The bomb is cooled to room temperature and opened. The crude solution is concentrated and the residue partitioned between water (200 mL) and hexanes (200 mL). The excess phenol is extracted into the hexane layer. The aqueous layer is extracted with ethyl acetate (3x200 mL) and the combined organic layers are washed once with water, dried over anhydrous sodium sulfate, and concentrated. The residue is columned on silica gel using methanol/methylene chloride 1:20 (which has 2% triethylamine) as the eluent. As the column fractions are concentrated a colorless solid forms which is collected to give the title compound as a white solid.

5'-O-dimethoxytrityl-2'-O-[2(2-N,N-dimethylaminoethoxy) ethyl)]-5-methyl uridine

[00141] To 0.5 g (1.3 mmol) of 2'-O-[2(2-N,N-dimethylaminoethoxy)ethyl)1-5-methyl uridine in anhydrous pyridine (8 mL), triethylamine (0.36 mL) and dimethoxytrityl chloride (DMT-Cl, 0.87 g, 2 eq.) are added and stirred for 1 hour. The reaction mixture is poured into water (200 mL) and extracted with CH_2Cl_2 (2x200 mL). The combined CH_2Cl_2 layers are washed with saturated $NaHCO_3$ solution, followed by saturated NaCl solution, and dried over anhydrous sodium sulfate. Evaporation of the solvent followed by silica gel chromatography using MeOH: CH_2Cl_2:Et_3N (20:1, v/v, with 1% triethylamine) gives the title compound.

5'-O-Dimethoxytrityl-2'-O-[2(2-N,N-dimethylaminoethoxy)ethyl)]-5-methyl uridine-3'-O-(cyanoethyl-N,N-diisopropyl)phosphoramidite

[00142] Diisopropylaminotetrazolide (0.6 g) and 2-cyanoethoxyN,N-diisopropyl phosphoramidite (1.1 mL, 2 eq.) are added to a solution of 5'-O-dimethoxytrityl-2'-O-[2(2-N,N-dimethylaminoethoxy)ethyl)]-5-methyluridine (2.17 g, 3 mmol) dissolved in CH_2Cl_2 (20 mL) under an atmosphere of argon. The reaction mixture is stirred overnight and the solvent evaporated. The resulting residue is purified by silica gel flash column chromatography with ethyl acetate as the eluent to give the title compound.

Example 2

Oligonucleotide synthesis

[00143] Unsubstituted and substituted phosphodiester (P=O) oligonucleotides are synthesized on an automated DNA synthesizer (Applied Biosystems model 380B) using standard phosphoramidite chemistry with oxidation by iodine.

[00144] Phosphorothioates (P=S) are synthesized as for the phosphodiester oligonucleotides except the standard oxidation bottle is replaced by 0.2 M solution of 3H-1,2-benzodithiole-3-one 1,1-dioxide in acetonitrile for the stepwise thiation of the phosphite linkages. The thiation wait step is increased to

68 sec and is followed by the capping step. After cleavage from the CPG column and deblocking in concentrated ammonium hydroxide at 55°C (18 h), the oligonucleotides are purified by precipitating twice with 2.5 volumes of ethanol from a 0.5 M NaCl solution. Phosphinate oligonucleotides are prepared as described in U.S. Patent 5,508,270, herein incorporated by reference.

[00145] Alkyl phosphonate oligonucleotides are prepared as described in U.S. Patent 4,469,863, herein incorporated by reference.

[00146] 3'-Deoxy-3'-methylene phosphonate oligonucleotides are prepared as described in U.S. Patents 5,610,289 or 5,625,050, herein incorporated by reference.

[00147] Phosphoramidite oligonucleotides are prepared as described in U.S. Patent, 5,256,775 or U.S. Patent 5,366,878, herein incorporated by reference.

[00148] Alkylphosphonothioate oligonucleotides are prepared as described in WO 94/17093 and WO 94/02499 herein incorporated by reference.

[00149] 3'-Deoxy-3'-amino phosphoramidate oligonucleotides are prepared as described in U.S. Patent 5,476,925, herein incorporated by reference.

[00150] Phosphotriester oligonucleotides are prepared as described in U.S. Patent 5,023,243, herein incorporated by reference.

[00151] Borano phosphate oligonucleotides are prepared as described in U.S. Patents 5,130,302 and 5,177,198, both herein incorporated by reference.

Example 3

Oligonucleoside Synthesis

[00152] Methylenemethylimino linked oligonucleosides, also identified as MMI linked oligonucleosides, methylenedimethylhydrazo linked oligonucleosides, also identified as MDH linked oligonucleosides, and methylenecarbonylamino linked oligonucleosides, also identified as amide-3 linked oligonucleosides, and methyleneaminocarbonyl linked oligonucleosides, also identified as amide-4 linked oligonucleosides, as well as mixed backbone compounds having, for instance, alternating MMI and P=O or P=S linkages are prepared as described in U.S. Patents 5,378,825; 5,386,023; 5,489,677; 5,602,240; and 5,610,289, all of which are herein incorporated by reference.

[00153] Formacetal and thioformacetal linked oligonucleosides are prepared as described in U.S. Patents 5,264,562 and 5,264,564, herein incorporated by reference.

[00154] Ethylene oxide linked oligonucleosides are prepared as described in U.S. Patent 5,223,618, herein incorporated by reference.

Example 4

PNA Synthesis

[00155] Peptide nucleic acids (PNAs) are prepared in accordance with any of the various procedures referred to in *Peptide Nucleic Acids* (PNA): *Synthesis, Properties and Potential Applications, Bioorganic & Medicinal Chemistry*, 1996, 4, 523. They may also be prepared in accordance with U.S. Patents 5,539,082; 5,700,922; and 5,719,262, herein incorporated by reference.

Example 5

Synthesis of Chimeric Oligonucleotides

[00156] Chimeric oligonucleotides, oligonucleosides, or mixed oligonucleotides/oligonucleosides of the invention can be of several different types. These include a first type wherein the "gap" segment of linked nucleosides is positioned between 5' and 3' "wing" segments of linked nucleosides and a second "open end" type wherein the "gap" segment is located at either the 3' or the 5' terminus of the oligomeric compound. Oligonucleotides of the first type are also known in the art as "gapmers" or gapped oligonucleotides. Oligonucleotides of the second type are also known in the art as "hemimers" or "wingmers".

[2'-O-Me]--[2'-deoxy]--[2'-O-Me] Chimeric Phosphorothioate Oligonucleotides

[00157] Chimeric oligonucleotides having 2'-O-alkyl phosphorothioate and 2'-deoxy phosphorothioate oligonucleotide segments are synthesized using an Applied Biosystems automated DNA synthesizer Model 380B, as above.

Oligonucleotides are synthesized using the automated synthesizer and 2'-deoxy-5'-dimethoxytrityl-3'-O-phosphoramidite for the DNA portion and 5'-dimethoxytrityl-2'-O-methyl-3'-O-phosphoramidite for 5' and 3' wings. The standard synthesis cycle is modified by increasing the wait step after the delivery of tetrazole and base to 600 s repeated four times for RNA and twice for 2'-O-methyl. The fully protected oligonucleotide is cleaved from the support and the phosphate group is deprotected in 3:1 ammonia/ethanol at room temperature overnight then lyophilized to dryness. Treatment in methanolic ammonia for 24 hrs at room temperature is then done to deprotect all bases and sample is again lyophilized to dryness. The pellet is resuspended in 1M TBAF in THF for 24 hrs at room temperature to deprotect the 2' positions. The reaction is then quenched with 1M TEAA and the sample is then reduced to 1/2 volume by rotovac before being desalted on a G25 size exclusion column. The oligo recovered is then analyzed spectrophotometrically for yield and for purity by capillary electrophoresis and by mass spectrometry.

[2'-O-(2-Methoxyethyl)]--[2'-deoxy]--[2'-O-(Methoxyethyl)] Chimeric Phosphorothioate Oligonucleotides

[00158] [2'-O-(2-methoxyethyl)]--[2'-deoxy]—[-2'-O-(methoxyethyl)] chimeric phosphorothioate oligonucleotides are prepared as per the procedure above for the 2'-O-methyl chimeric oligonucleotide, with the substitution of phorothioate oligonucleotides are prepared as per the procedure above for 2'-O-(methoxyethyl) amidites for the 2'-O-methyl amidites.

[2'-O-(2-Methoxyethyl)Phosphodiester]--[2'-deoxy Phosphorothioate]--[2'-O-(2-Methoxyethyl)] Phosphodiester] Chimeric Oligonucleotides

[00159] [2'-O-(2-methoxyethyl phosphodiester]--[2'-deoxy phosphorothioate]--[2'-O-(methcixyethyl) phosphodiester] chimeric oligonucleotides are prepared as per the above procedure for the 2'-O-methyl chimeric oligonucleotide with the substitution of 2'-O-(methoxyethyl) amidites for the 2'-O-methyl amidites, oxidization with iodine to generate the phosphodiester internucleotide linkages within the wing portions of the chimeric structures and sulfurization utilizing 3,H-1,2 benzodithiole-3-one 1,1 dioxide

(Beaucage Reagent) to generate the phosphorothioate internucleotide linkages for the center gap.

[00160] Other chimeric oligonucleotides, chimeric oligonucleosides, and mixed chimeric oligonucleotides/oligonucleosides are synthesized according to United States patent 5,623,065, herein incorporated by reference.

Example 6

Oligonucleotide Isolation

[00161] After cleavage from the controlled pore glass column (Applied Biosystems) and deblocking in concentrated ammonium hydroxide at 55°C for 18 hours, the oligonucleotides or oligonucleosides are purified by precipitation twice out of 0.5 M NaCl with 2.5 volumes ethanol. Synthesized oligonucleotides are analyzed by polyacrylamide gel electrophoresis on denaturing gels and judged to be at least 85% full-length material. The relative amounts of phosphorothioate and phosphodiester linkages obtained in synthesis are periodically checked by "P nuclear magnetic resonance spectroscopy, and for some studies oligonucleotides are purified by HPLC, as described by Chiang et al., *J. Biol. Chem.* 1991, 266, 18162-18171.

Example 7

Oligonucleotide Synthesis - 96 Well Plate Format

[00162] Oligonucleotides are synthesized via solid phase P(III) phosphoramidite chemistry on an automated synthesizer capable of assembling 96 sequences simultaneously in a standard 96 well format. Phosphodiester internucleotide linkages are afforded by oxidation with aqueous iodine. Phosphorothioate internucleotide linkages are generated by sulfurization utilizing 3,H-1,2 benzodithiole-3-one 1,1 dioxide (Beaucage Reagent) in anhydrous acetonitrile. Standard base-protected beta-cyanoethyldiisopropyl phosphoramidites can be purchased from commercial vendors (e.g. PE-Applied Biosystems, Foster City, CA, or Pharmacia, Piscataway, NJ). Non-standard

nucleosides are synthesized as per known literature or patented methods. They are utilized as base protected betacyanoethyldiisopropyl phosphoramidites.

[00163] Oligonucleotides are cleaved from support and deprotected with concentrated NH_4OH at elevated temperature (55-60°C) for 12-16 hours and the released product then dried in vacuo. The dried product is then re-suspended in sterile water to afford a master plate from which all analytical and test plate samples are then diluted utilizing robotic pipettors.

Example 8

Oligonucleotide Analysis - 96 Well Plate Format

[00164] The concentration of oligonucleotide in each well is assessed by dilution of samples and UV absorption spectroscopy. The full-length integrity of the individual products is evaluated by capillary electrophoresis (CE) in either the 96 well format (Beckman P/ACE™ MDQ) or, for individually prepared samples, on a commercial CE apparatus (e.g., Beckman P/ACE™ 5000, ABI 270). Base and backbone composition is confirmed by mass analysis of the compounds utilizing electrospray-mass spectroscopy. All assay test plates are diluted from the master plate using single and multi-channel robotic pipettors. Plates are judged to be acceptable if at least 85% of the compounds on the plate are at least 85% full length.

Example 9

Cell culture and oligonucleotide treatment

[00165] The effect of antisense compounds on target nucleic acid expression can be tested in any of a variety of cell types provided that the target nucleic acid is present at measurable levels. This can be routinely determined using, for example, PCR or Northern blot analysis. The following 6 cell types are provided for illustrative purposes, but other cell types can be routinely used, provided that the target is expressed in the cell type chosen. This can be readily determined by methods routine in the art, for example Northern blot analysis, Ribonuclease protection assays, or RT-PCR.

T-24 cells:

[00166] The human transitional cell bladder carcinoma cell line T-24 is obtained from the American Type Culture Collection (ATCC) (Manassas, VA). T-24 cells are routinely cultured in complete McCoy's 5A basal media (Gibco/Life Technologies, Gaithersburg, MD) supplemented with 10% fetal calf serum (Gibco/Life Technologies, Gaithersburg, MD), penicillin 100 units per mL, and streptomycin 100 micrograms per mL (Gibco/Life Technologies, Gaithersburg, MD). Cells are routinely passaged by trypsinization and dilution when they reached 90% confluence. Cells are seeded into 96-well plates (Falcon-Primaria #3872) at a density of 7000 cells/well for use in RT-PCR analysis.

[00167] For Northern blotting or other analysis, cells may be seeded onto 100 mm or other standard tissue culture plates and treated similarly, using appropriate volumes of medium and oligonucleotide.

A549 cells:

[00168] The human lung carcinoma cell line A549 can be obtained from the American Type Culture Collection (ATCC) (Manassas, VA). A549 cells are routinely cultured in DMEM basal media (Gibco/Life Technologies, Gaithersburg, MD) supplemented with 10% fetal calf serum (Gibco/Life Technologies, Gaithersburg, MD), penicillin 100 units per mL, and streptomycin 100 micrograms per mL (Gibco/Life Technologies, Gaithersburg, MD). Cells are routinely passaged by trypsinization and dilution when they reached 90% confluence.

NHDF cells:

[00169] Human neonatal dermal fibroblast (NHDF) can be obtained from the Clonetics Corporation (Walkersville MD). NHDFs are routinely maintained in Fibroblast Growth Medium (Clonetics Corporation, Walkersville MD) supplemented as recommended by the supplier. Cells are maintained for up to 10 passages as recommended by the supplier.

HEK cells:

[00170] Human embryonic keratinocytes (HEK) can be obtained from the Clonetics Corporation (Walkersville MD). HEKs are routinely maintained in Keratinocyte Growth Medium (Clonetics Corporation, Walkersville MD) formulated as recommended by the supplier. Cells are routinely maintained for up to 10 passages as recommended by the supplier.

MCF-7 cells:

[00171] The human breast carcinoma cell line MCF-7 is obtained from the American Type Culture Collection (Manassas, VA). MCF-7 cells are routinely cultured in DMEM low glucose (Gibco/Life Technologies, Gaithersburg, MD) supplemented with 10% fetal calf serum (Gibco/Life Technologies, Gaithersburg, MD). Cells are routinely passaged by trypsinization and dilution when they reached 90% confluence. Cells are seeded into 96-well plates (Falcon-Primaria #3872) at a density of 7000 cells/well for use in RT-PCR analysis.

[00172] For Northern blotting or other analyses, cells may be seeded onto 100 mm or other standard tissue culture plates and treated similarly, using appropriate volumes of medium and oligonucleotide.

LA4 cells:

[00173] The mouse lung epithelial cell line LA4 is obtained from the American Type Culture Collection (Manassas, VA). LA4 cells are routinely cultured in F12K medium (Gibco/Life Technologies, Gaithersburg, MD) supplemented with 15% fetal calf serum (Gibco/Life Technologies, Gaithersburg, MD). Cells are routinely passaged by trypsinization and dilution when they reached 90% confluence. Cells are seeded into 96-well plates (Falcon-Primaria #3872) at a density of 3000-6000 cells/ well for use in RT-PCR analysis.

[00174] For Northern blotting or other analyses, cells may be seeded onto 100 mm or other standard tissue culture plates and treated similarly, using appropriate volumes of medium and oligonucleotide.

Treatment with antisense compounds:

[00175] When cells reached 80% confluence, they are treated with oligonucleotide. For cells grown in 96-well plates, wells are washed once with 200 µL OPTI-MEM^{tm}-1 reduced-serum medium (Gibco BRL) and then treated with 130 µL of OPTI-MEMTM™-1 containing 3.75 µg/mL LIPOFECTIN™ (Gibco BRL) and the desired concentration of oligonucleotide. After 4-7 hours of treatment, the medium is replaced with fresh medium. Cells are harvested 16-24 hours after oligonucleotide treatment.

[00176] The concentration of oligonucleotide used varies from cell line to cell line. To determine the optimal oligonucleotide concentration for a particular cell line, the cells are treated with a positive control oligonucleotide at a range of concentrations.

Example 10

Analysis of oligonucleotide inhibition of FXR expression

[00177] Antisense modulation of FXR expression can be assayed in a variety of ways known in the art. For example, FXR mRNA levels can be quantitated by, e.g., Northern blot analysis, competitive polymerase chain reaction (PCR), or real-time PCR (RT-PCR). Real-time quantitative PCR is presently preferred. RNA analysis can be performed on total cellular RNA or poly(A)+ mRNA. Methods of RNA isolation are taught in, for example, Ausubel, F.M. et al., *Current Protocols in Molecular Biology*, Volume 1, pp. 4.1.1-4.2.9 and 4.5.1-4.5.3, John Wiley & Sons, Inc., 1993. Northern blot analysis is routine in the art and is taught in, for example, Ausubel, F.M. et al., *Current Protocols in Molecular Biology*, Volume 1, pp. 4.2.1-4.2.9, John Wiley & Sons, Inc., 1996. Real-time quantitative (PCR) can be conveniently accomplished using the commercially available ABI PRISM™ 7700 Sequence Detection System, available from PE-Applied Biosystems, Foster City, CA and used according to manufacturer's instructions. Prior to quantitative PCR analysis, primer-probe sets specific to the target gene being measured are evaluated for their ability to be "multiplexed" with a GAPDH amplification reaction. In multiplexing, both the target gene and the internal standard gene GAPDH are amplified

concurrently in a single sample. In this analysis, mRNA isolated from untreated cells is serially diluted. Each dilution is amplified in the presence of primer-probe sets specific for GAPDH only, target gene only ("single-plexing"), or both (multiplexing). Following PCR amplification, standard curves of GAPDH and target mRNA signal as a function of dilution are generated from both the single-plexed and multiplexed samples. If both the slope and correlation coefficient of the GAPDH and target signals generated from the multiplexed samples fall within 10% of their corresponding values generated from the single-plexed samples, the primer-probe set specific for that target is deemed as multiplexable. Other methods of PCR are also known in the art.

[00178] Protein levels of FXR can be quantitated in a variety of ways well known in the art, such as immunoprecipitation, Western blot analysis (immunoblotting), ELISA or fluorescence-activated cell sorting (FACS). Antibodies directed to FXR can be identified and obtained from a variety of sources, such as the MSRS catalog of antibodies (Aerie Corporation, Birmingham, MI), or can be prepared via conventional antibody generation methods. Methods for preparation of polyclonal antisera are taught in, for example, Ausubel, F.M. et al., *Current Protocols in Molecular Biology*, Volume 2, pp. 11.12.1-11.12.9, John Wiley & Sons, Inc., 1997. Preparation of monoclonal antibodies is taught in, for example, Ausubel, F.M. et al., *Current Protocols in Molecular Biology*, Volume 2, pp. 11.4.1-11.11.5, John Wiley Sons, Inc., 1997.

[00179] Immunoprecipitation methods are standard in the art and can be found at, for example, Ausubel, F.M. et al., *Current Protocols in Molecular Biology*, Volume 2, pp. 10.16.110.16.11, John Wiley & Sons, Inc., 1998. Western blot (immunoblot) analysis is standard in the art and can be found at, for example, Ausubel, F.M. et al., *Current Protocols in Molecular Biology*, Volume 2, pp. 10.8.1-10.8.21, John Wiley Sons, Inc., 1997. Enzyme-linked immunosorbent assays (ELISA) are standard in the art and can be found at, for example, Ausubel, F.M. et al., *Current Protocols in Molecular Biology*, Volume 2, pp. 11.2.1-11.2.22, John Wiley & Sons, Inc., 1991.

Example 11

Poly(A)+ mRNA isolation

[00180] Poly(A)+ mRNA is isolated according to Miura et al., *Clin. Chem.*, 1996, 42, 1758-1764. Other methods for poly(A)+ mRNA isolation are taught in, for example, Ausubel, F.M. et al., *Current Protocols in Molecular Biology*, Volume 1, pp. 4.5.1-4.5.3, John Wiley & Sons, Inc., 1993. Briefly, for cells grown on 96-well plates, growth medium is removed from the cells and each well is washed with 200 μL cold PBS. 60μL lysis buffer (10 mM Tris-HCl, pH 7.6, 1 mM EDTA, 0.5 M NaCl, 0.5% NP-40, 20 mM vanadyl-ribonucleoside complex) is added to each well, the plate is gently agitated and then incubated at room temperature for five minutes. 55 μL of lysate is transferred to Oligo d(T) coated 96-well plates (AGCT Inc., Irvine CA). Plates are incubated for 60 minutes at room temperature, washed 3 times with 200 μL of wash buffer (10 mM Tris-HC1 pH 7.6, 1 mM EDTA, 0.3 M NaCl). After the final wash, the plate is blotted on paper towels to remove excess wash buffer and then air-dried for 5 minutes. 60 pL of elution buffer (5 mM Tris-HCl pH 7.6), preheated to 70°C is added to each well, the plate is incubated on a 90°C hot plate for 5 minutes, and the eluate is then transferred to a fresh 96-well plate.

[00181] Cells grown on 100 mm or other standard plates may be treated similarly, using appropriate volumes of all solutions.

Example 12

Total RNA Isolation

[00182] Total mRNA is isolated using an RNEASY 96™ kit and buffers purchased from Qiagen Inc. (Valencia CA) following the manufacturer's recommended procedures. Briefly, for cells grown on 96-well plates, growth medium is removed from the cells and each well is washed with 200 μL cold PBS. 100 μL Buffer RLT is added to each well and the plate vigorously agitated for 20 seconds. 100 μL of 70% ethanol is then added to each well and the contents mixed by pipetting three times up and down. The samples are then transferred to the RNEASY 96™ well plate attached to a QIAVAC™ manifold

fitted with a waste collection tray and attached to a vacuum source. Vacuum is applied for 15 seconds. 1 mL of Buffer RW1 is added to each well of the RNEASY 96™ plate and the vacuum again applied for 15 seconds. 1 mL of Buffer RPE is then added to each well of the RNEASY 96™ plate and the vacuum applied for a period of 15 seconds. The Buffer RPE wash is then repeated and the vacuum is applied for an additional 10 minutes. The plate is then removed from the QIAVAC™ manifold and blotted dry on paper towels. The plate is then re-attached to the QIAVAC™ manifold fitted with a collection tube rack containing 1.2 mL collection tubes. RNA is then eluted by pipetting 60μL water into each well, incubating one minute, and then applying the vacuum for 30 seconds. The elution step is repeated with additional 60μL water.

[00183] The repetitive pipetting and elution steps may be automated using a QIAGEN Bio-Robot 9604 (Qiagen, Inc., Valencia CA). Essentially, after lysing of the cells on the culture plate, the plate is transferred to the robot deck where the pipetting, DNase treatment and elution steps are carried out.

Example 13

Real-time Quantitative PCR Analysis of FXR mRNA Levels

[00184] Quantitation of FXR mRNA levels is determined by real-time quantitative PCR using the ABI PRISM™ 7700 Sequence Detection System (PE-Applied Biosystems, Foster City, CA) according to manufacturer's instructions. This is a closed-tube, non-gel-based, fluorescence detection system which allows high-throughput quantitation of polymerase chain reaction (PCR) products in real-time. As opposed to standard PCR, in which amplification products are quantitated after the PCR is completed, products in real-time quantitative PCR are quantitated as they accumulate. This is accomplished by including in the PCR reaction an oligonucleotide probe that anneals specifically between the forward and reverse PCR primers, and contains two fluorescent dyes. A reporter dye (e.g., JOE, FAM™, or VIC, obtained from either Operon Technologies Inc., Alameda, CA or PE-Applied Biosystems, Foster City, CA) is attached to the 5' end of the probe and a quencher dye (e.g., TAMRA, obtained from either Operon Technologies Inc., Alameda, CA or PE-Applied

Biosystems, Foster City, CA) is attached to the 3' end of the probe. When the probe and dyes are intact, reporter dye emission is quenched by the proximity of the 3' quencher dye. During amplification, annealing of the probe to the target sequence creates a substrate that can be cleaved by the 5'-exonuclease activity of Taq polymerase. During the extension phase of the PCR amplification cycle, cleavage of the probe by Taq polymerase releases the reporter dye from the remainder of the probe (and hence from the quencher moiety) and a sequence-specific fluorescent signal is generated. With each cycle, additional reporter dye molecules are cleaved from their respective probes, and the fluorescence intensity is monitored at regular intervals by laser optics built into the ABI PRISM™ 7700 Sequence Detection System. In each assay, a series of parallel reactions containing serial dilutions of mRNA from untreated control samples generates a standard curve that is used to quantitate the percent inhibition after antisense oligonucleotide treatment of test samples.

[00185] PCR reagents can be obtained from PE-Applied Biosystems, Foster City, CA. RT-PCR reactions are carried out by adding 25µL PCR cocktail (1x TAQMAN™ buffer A, 5.5 MM $MgCl_2$, 300 µM each of dATP, dCTP and dGTP, 600 µM of dUTP, 100 nM each of forward primer, reverse primer, and probe, 20 Units RNAse inhibitor, 1.25 Units AMPLITAQ GOLD™, and 12.5 Units MuLV reverse transcriptase) to 96 well plates containing 25 µL poly(A) mRNA solution. The RT reaction is carried out by incubation for 30 minutes at 48°C. Following a 10 minute incubation at 95°C to activate the AMPLITAQ GOLD™, 40 cycles of a two-step PCR protocol are carried out: 95°C for 15 seconds (denaturation) followed by 60°C for 1.5 minutes (annealing/extension).

[00186] Probes and primers to human FXR were designed to hybridize to a human FXR sequence, using published sequence, information (NM_005123, incorporated herein as Figure 1). For human FXR the PCR primers were:
forward primer: CTGGGTCGCCTGACTGAATT SEQ ID NO:2139
reverse primer: GGTCGTTTACTCTCCATGACATCA SEQ ID NO:2140 and the PCR probe is: FAM™- CGGACATTCAATCATCACCACGCTGAG SEQ ID NO:2141-TAMRA where FAM™ (PE-Applied Biosystems, Foster City, CA) is the fluorescent reporter dye) and TAMRA (PE-Applied Biosystems, Foster City,

CA) is the quencher dye. For human cyclophilin the PCR primers were: forward primer: CCCACCGTGTTCTTCGACAT SEQ ID NO:2142
reverse primer: TTTCTGCTGTCTTTGGGACCTT SEQ ID NO:2143 and the PCR probe is: 5' JOE- CGCGTCTCCTTTGAGCTGTTTGCA SEQ ID NO:2144- TAMRA 3' where JOE (PE-Applied Biosystems, Foster City, CA) is the fluorescent reporter dye) and TAMRA (PE-Applied Biosystems, Foster City, CA) is the quencher dye.

Example 14

Antisense inhibition of human FXR expression by chimeric phosphorothioate oligonucleotides having 2'-MOE wings and a deoxy gap

[00187] In accordance with the present invention, a series of oligonucleotides are designed to target different regions of the human FXR RNA, using published sequences (NM_005123, incorporated herein as Figure 1). The oligonucleotides are shown in Table 1. "Position" indicates the first (5'-most) nucleotide number on the particular target sequence to which the oligonucleotide binds. The indicated parameters for each oligo were predicted using RNAstructure 3.7 by David H. Mathews, Michael Zuker, and Douglas H. Turner. The parameters are described either as free energy (The energy that is released when a reaction occurs. The more negative the number, the more likely the reaction will occur. All free energy units are in kcal/mol. or melting temperature (the temperature at which two anneal strands of polynucleic acid separate. The higher the temperature, greater the affinity between the 2 strands.) When designing an antisense oligonucleotide (oligomers) that will bind with high affinity, it is desirable to consider the structure of the target RNA strand and the antisense oligomer. Specifically, for an oligomer to bind tightly (in the table described as 'duplex formation'), it should be complementary to a stretch of target RNA that has little self-structure (in the table the free energy of which is described as 'target structure'). Also, the oligomer should have little self-structure, either intramolecular (in the table the free energy of which is described as 'intramolecular oligo') or bimolecular (in the table the free energy of which is described as 'intermolecular oligo'). Breaking up any self-structure

amounts to a binding penalty. All compounds in Table 1 are chimeric oligonucleotides ("gapmers") 20 nucleotides in length, composed of a central "gap" region consisting of ten 2'deoxynucleotides, which is flanked on both sides (5' and 3' directions) by four-nucleotide "wings". The wings are composed of 2'-methoxyethyl (2'-MOE) nucleotides. The internucleoside (backbone) linkages are phosphorothioate (P=S) throughout the oligonucleotide. Cytidine residues in the 2'-MOE wings are 5-methylcytidines. All cytidine residues are 5-methylcytidines.

TABLE 1

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intra-molecular oligo	kcal/mol Inter-molecular oligo
1132	AGGCATCCTCTGTTTGTTAT SEQ.ID.NO:1	-21.6	-24.7	73.8	-3.1	0	-4
1136	CCTGAGGCATCCTCTGTTTG SEQ.ID.NO:2	-21.6	-27.2	77.4	-3.1	-2.5	-7.9
682	CGCGCCCATGCGGGGCTTCT SEQ.ID.NO:3	-21.5	-34.2	84.9	-8.2	-4.5	-11.3
684	GACGCGCCCATGCGGGGCTT SEQ.ID.NO:4	-21.5	-33.7	83.3	-8.2	-4	-11.8
1131	GGCATCCTCTGTTTGTTATA SEQ.ID.NO:5	-21.3	-24.4	72.8	-3.1	0	-4
882	CGACACTCTTGACACTTTCT SEQ.ID.NO:6	-21	-22.9	67	-1.9	0	-2.1
685	TGACGCGCCCATGCGGGGCT SEQ.ID.NO:7	-20.9	-33.6	82.7	-8.2	-4.5	-11.8
681	GCGCCCATGCGGGGCTTCTT SEQ.ID.NO:8	-20.8	-33.5	85.9	-8.2	-4.5	-11.3
683	ACGCGCCCATGCGGGGCTTC SEQ.ID.NO:9	-20.8	-33.5	83.7	-8.2	-4.5	-11.8
686	CTGACGCGCCCATGCGGGGC SEQ.ID.NO:10	-20.8	-33.6	82.7	-9.1	-3.7	-11.1
1135	CTGAGGCATCCTCTGTTTGT SEQ.ID.NO:11	-20.8	-26.4	77.4	-3.1	-2.5	-7.9
678	CCCATGCGGGGCTTCTTTGT SEQ.ID.NO:12	-20.7	-30.4	81.7	-8.2	-1.4	-6.8
848	CCATCACACAGTTGCCCCCG SEQ.ID.NO:13	-20.5	-31.5	80.3	-11	0	-3
883	TCGACACTCTTGACACTTTC SEQ.ID.NO:14	-20.5	-22.4	66.6	-1.9	0	-4.2
845	TCACACAGTTGCCCCCGTTT SEQ.ID.NO:15	-20.4	-30.2	80.1	-9.8	0	-3
1133	GAGGCATCCTCTGTTTGTTA SEQ.ID.NO:16	-20.4	-25.3	75.3	-3.1	-1.8	-7.1
881	GACACTCTTGACACTTTCTT SEQ.ID.NO:17	-20.3	-22.2	67.1	-1.9	0	-2.3
884	GTCGACACTCTTGACACTTT SEQ.ID.NO:18	-20.3	-23.2	68.3	-1.9	-0.7	-8.8
844	CACACAGTTGCCCCCGTTTT SEQ.ID.NO:19	-20.1	-29.9	78.8	-9.8	0	-3
1130	GCATCCTCTGTTTGTTATAT SEQ.ID.NO:20	-20.1	-23.2	70	-3.1	0	-3.4
1138	TTCCTGAGGCATCCTCTGTT SEQ.ID.NO:21	-20.1	-27.6	79.5	-5.7	-1.8	-7.2
219	GCAGTGTTCACTTTGAGCTA SEQ.ID.NO:22	-20	-24.4	73.6	-3.9	-0.1	-7.9
1134	TGAGGCATCCTCTGTTTGTT SEQ.ID.NO:23	-20	-25.6	75.7	-3.1	-2.5	-7.9
220	AGCAGTGTTCACTTTGAGCT SEQ.ID.NO:24	-19.9	-24.7	74.6	-3.9	-0.8	-8
1143	GTTATTTCCTGAGGCATCCT SEQ.ID.NO:25	-19.8	-26.1	75.6	-5.7	-0.3	-5.4
677	CCATGCGGGGCTTCTTTGTT SEQ.ID.NO:26	-19.7	-28.5	78.7	-8.2	-0.3	-4.3

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intra-molecular oligo	kcal/mol Inter-molecular oligo
847	CATCACACAGTTGCCCCCGT SEQ.ID.NO:27	-19.7	-30.7	80.3	-11	0	-3
885	AGTCGACACTCTTGACACTT SEQ.ID.NO:28	-19.6	-23.1	68.2	-1.9	-1.5	-9.5
1144	TGTTATTTCCTGAGGCATCC SEQ.ID.NO:29	-19.5	-25.2	73.4	-5.7	0	-5.4
315	TGCACTTTCTTTATGGTGGT SEQ.ID.NO:30	-19.4	-23.8	71.5	-3.7	-0.5	-4.7
846	ATCACACAGTTGCCCCCGTT SEQ.ID.NO:31	-19.4	-30.1	79.7	-10.7	0	-3
906	CCCATCTCTTTGCATTTCCT SEQ.ID.NO:32	-19.4	-27.5	77.2	-8.1	0	-5.1
1139	TTTCCTGAGGCATCCTCTGT SEQ.ID.NO:33	-19.4	-27.6	79.5	-5.7	-2.5	-7.9
1655	GTAATTCAGTCAGGCGACCC SEQ.ID.NO:34	-19.4	-26.3	73.9	-5.5	-1.3	-5.4
886	TAGTCGACACTCTTGACACT SEQ.ID.NO:35	-19.2	-22.7	67.2	-1.9	-1.5	-9.5
314	GCACTTTCTTTATGGTGGTC SEQ.ID.NO:36	-19.1	-24.2	73.4	-4.4	-0.5	-4.5
680	CGCCCATGCGGGGCTTCTTT SEQ.ID.NO:37	-19.1	-31.8	82.2	-8.2	-4.5	-11.3
907	TCCCATCTCTTTGCATTTCC SEQ.ID.NO:38	-18.9	-27	76.9	-8.1	0	-5.1
679	GCCCATGCGGGGCTTCTTTG SEQ.ID.NO:39	-18.8	-31	82.5	-8.2	-4	-11
2138	TTTTTTTTTCTGTTGCCATT SEQ.ID.NO:40	-18.8	-22	66.8	-3.2	0	-3
221	AAGCAGTGTTCACTTTGAGC SEQ.ID.NO:41	-18.7	-23.1	69.8	-3.9	0	-7.9
1979	GCCAATTAGAATGCAGGATT SEQ.ID.NO:42	-18.7	-21.9	63.6	-3.2	0	-5.5
2134	TTTTTCTGTTGCCATTATGT SEQ.ID.NO:43	-18.7	-22.5	68	-3.8	0	-3
687	GCTGACGCGCCCATGCGGGG SEQ.ID.NO:44	-18.6	-33.6	82.7	-12.2	-2.8	-11.1
699	TTGATCCTCCCTGCTGACGC SEQ.ID.NO:45	-18.6	-29.4	79	-10.3	-0.1	-4.5
843	ACACAGTTGCCCCCGTTTTT SEQ.ID.NO:46	-18.6	-29.3	78.2	-10.7	0	-3
917	CAGCCAACATTCCCATCTCT SEQ.ID.NO:47	-18.6	-27.2	74.9	-8.6	0	-3.2
313	CACTTTCTTTATGGTGGTCT SEQ.ID.NO:48	-18.4	-23.3	70.9	-4.9	0	-3.9
887	TTAGTCGACACTCTTGACAC SEQ.ID.NO:49	-18.4	-21.9	65.6	-1.9	-1.5	-9.5
984	TCTGCATGCTGCTTCACATT SEQ.ID.NO:50	-18.4	-25.4	73.9	-5.2	-1.8	-9.7
2137	TTTTTTTTCTGTTGCCATTA SEQ.ID.NO:51	-18.4	-21.6	65.8	-3.2	0	-3
216	GTGTTCACTTTGAGCTATGT SEQ.ID.NO:52	-18.3	-23.1	70.8	-3.9	-0.8	-5.1
1129	CATCCTCTGTTTGTTATATG SEQ.ID.NO:53	-18.3	-21.4	65.4	-3.1	0	-2.4
1982	CTTGCCAATTAGAATGCAGG	-18.3	-22.2	64.1	-3.2	-0.5	-5.5

		kcal/ mol	kcal/ mol	deg C	kcal/ mol	kcal/ mol	kcal/ mol
						Intra-	Inter-
			duplex		target	mole-	mole-
		total	forma-	Tm of	struc-	cular	cular
position	oligo	binding	tion	Duplex	ture	oligo	oligo
	SEQ.ID.NO:54						
2136	TTTTTTTCTGTTGCCATTAT SEQ.ID.NO:55	-18.3	-21.5	65.4	-3.2	0	-3
608	GCATACGCCTGAGTTCATAT SEQ.ID.NO:56	-18.2	-24.6	70.2	-6.4	0	-3.4
849	TCCATCACACAGTTGCCCCC SEQ.ID.NO:57	-18.2	-31.1	82.4	-12.9	0	-3
889	CCTTAGTCGACACTCTTGAC SEQ.ID.NO:58	-18.2	-23.9	69.6	-5	0	-8.7
890	TCCTTAGTCGACACTCTTGA SEQ.ID.NO:59	-18.2	-24.1	70.6	-5	0	-9.5
1128	ATCCTCTGTTTGTTATATGA SEQ.ID.NO:60	-18.2	-21.3	65.6	-3.1	0	-2.4
1140	ATTTCCTGAGGCATCCTCTG SEQ.ID.NO:61	-18.2	-26.4	75.8	-5.7	-2.5	-7.9
2135	TTTTTTCTGTTGCCATTATG SEQ.ID.NO:62	-18.2	-21.4	65	-3.2	0	-3
691	CCCTGCTGACGCGCCCATGC SEQ.ID.NO:63	-18.1	-34.1	84	-14.7	-1.2	-8.2
918	TCAGCCAACATTCCCATCTC SEQ.ID.NO:64	-18.1	-26.7	74.6	-8.6	0	-3.2
983	CTGCATGCTGCTTCACATTT SEQ.ID.NO:65	-18.1	-25.1	72.6	-5.2	-1.8	-9.7
1122	TGTTTGTTATATGAATCCAT SEQ.ID.NO:66	-18.1	-19.1	59.1	-0.9	0	-2.6
916	AGCCAACATTCCCATCTCTT SEQ.ID.NO:67	-18	-26.6	74.2	-8.6	0	-3.2
981	GCATGCTGCTTCACATTTTT SEQ.ID.NO:68	-18	-24.4	71.5	-5.2	-1.1	-8.9
1137	TCCTGAGGCATCCTCTGTTT SEQ.ID.NO:69	-18	-27.6	79.5	-7.1	-2.5	-7.9
1651	TTCAGTCAGGCGACCCAGGA SEQ.ID.NO:70	-18	-28.6	78.8	-9.2	-1.3	-5.9
1980	TGCCAATTAGAATGCAGGAT SEQ.ID.NO:71	-18	-21.8	63.2	-3.2	-0.3	-5.5
1981	TTGCCAATTAGAATGCAGGA SEQ.ID.NO:72	-18	-21.9	63.5	-3.2	-0.5	-5.5
607	CATACGCCTGAGTTCATATA SEQ.ID.NO:73	-17.9	-22.5	65.5	-4.6	0	-3.3
1141	TATTTCCTGAGGCATCCTCT SEQ.ID.NO:74	-17.9	-26.1	75.4	-5.7	-2.5	-7.9
1142	TTATTTCCTGAGGCATCCTC SEQ.ID.NO:75	-17.9	-25.3	73.8	-5.7	-1.7	-6.9
218	CAGTGTTCACTTTGAGCTAT SEQ.ID.NO:76	-17.8	-22.6	68.9	-3.9	-0.8	-6.8
807	TTTTTGGTAATGCTTCTCCT SEQ.ID.NO:77	-17.8	-23.2	69.1	-5.4	0	-3.6
842	CACAGTTGCCCCCGTTTTTA SEQ.ID.NO:78	-17.8	-28.8	77.1	-11	0	-3
919	TTCAGCCAACATTCCCATCT SEQ.ID.NO:79	-17.8	-26.4	73.4	-8.6	0	-3.2
1654	TAATTCAGTCAGGCGACCCA SEQ.ID.NO:80	-17.8	-25.8	71.7	-6.6	-1.3	-5.4
2133	TTTTCTGTTGCCATTATGTT SEQ.ID.NO:81	-17.8	-22.5	68	-4.7	0	-3

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intra-molecular oligo	kcal/mol Inter-molecular oligo
850	ATCCATCACACAGTTGCCCC SEQ.ID.NO:82	-17.7	-29.1	79	-11.4	0	-3
1796	ATGAGAGAGAAAAAGGAGCT SEQ.ID.NO:83	-17.7	-18.1	55.9	0	0	-5
880	ACACTCTTGACACTTTCTTC SEQ.ID.NO:84	-17.6	-22	67.4	-4.4	0	-2.3
1941	CACAATGTAGAGAAAGTTGT SEQ.ID.NO:85	-17.6	-18.1	56.7	0	-0.2	-4.4
222	GAAGCAGTGTTCACTTTGAG SEQ.ID.NO:86	-17.5	-21.9	66.7	-3.9	0	-7.9
316	ATGCACTTTCTTTATGGTGG SEQ.ID.NO:87	-17.5	-22.6	68	-4.4	-0.5	-5.5
878	ACTCTTGACACTTTCTTCGC SEQ.ID.NO:88	-17.5	-23.7	70.1	-6.2	0	-2.7
905	CCATCTCTTTGCATTTCCTT SEQ.ID.NO:89	-17.5	-25.6	73.9	-8.1	0	-5.1
980	CATGCTGCTTCACATTTTTT SEQ.ID.NO:90	-17.5	-22.7	67.5	-5.2	0	-6
1127	TCCTCTGTTTGTTATATGAA SEQ.ID.NO:91	-17.5	-20.6	63.3	-3.1	0	-2.4
1299	CCTTTCAGCAAAGCAATCTG SEQ.ID.NO:92	-17.5	-22.4	64.8	-4	-0.8	-4.7
1722	GGGGTAAACTTGTGGTCGTT SEQ.ID.NO:93	-17.5	-24.4	70.7	-6.9	0	-3.4
1723	TGGGGTAAACTTGTGGTCGT SEQ.ID.NO:94	-17.4	-24.3	70.1	-6.9	0	-3
1724	GTGGGGTAAACTTGTGGTCG SEQ.ID.NO:95	-17.4	-24.3	70.1	-6.9	0	-2.5
605	TACGCCTGAGTTCATATATT SEQ.ID.NO:96	-17.3	-21.9	64.7	-4.6	0	-3.6
692	TCCCTGCTGACGCGCCCATG SEQ.ID.NO:97	-17.3	-32.7	81.7	-14.7	-0.5	-7.7
841	ACAGTTGCCCCCGTTTTTAC SEQ.ID.NO:98	-17.3	-28.3	76.7	-11	0	-3
915	GCCAACATTCCCATCTCTTT SEQ.ID.NO:99	-17.3	-26.7	74.2	-9.4	0	-2
982	TGCATGCTGCTTCACATTTT SEQ.ID.NO:100	-17.3	-24.3	71	-5.2	-1.8	-9.7
215	TGTTCACTTTGAGCTATGTT SEQ.ID.NO:101	-17.2	-22	67.6	-3.9	-0.8	-5.1
606	ATACGCCTGAGTTCATATAT SEQ.ID.NO:102	-17.2	-21.8	64.3	-4.6	0	-3.3
979	ATGCTGCTTCACATTTTTTC SEQ.ID.NO:103	-17.2	-22.4	67.9	-5.2	0	-6
217	AGTGTTCACTTTGAGCTATG SEQ.ID.NO:104	-17.1	-21.9	67.5	-3.9	-0.8	-6.6
312	ACTTTCTTTATGGTGGTCTT SEQ.ID.NO:105	-17.1	-22.7	70	-5.6	0	-2.2
838	GTTGCCCCCGTTTTTACACT SEQ.ID.NO:106	-17.1	-29.2	78.2	-11.4	-0.4	-3.4
1067	GTTCAGTTTTCTCCCTGCAT SEQ.ID.NO:107	-17.1	-27	79.1	-9.9	0	-4.9
1068	AGTTCAGTTTTCTCCCTGCA SEQ.ID.NO:108	-17.1	-27	79.5	-9.9	0	-4.7
1126	CCTCTGTTTGTTATATGAAT	-17.1	-20.2	61.8	-3.1	0	-2.4

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intra-molecular oligo	kcal/mol Inter-molecular oligo
	SEQ.ID.NO:109						
1983	GCTTGCCAATTAGAATGCAG SEQ.ID.NO:110	-17.1	-22.8	65.6	-5	-0.5	-5.5
665	TCTTTGTTACAGGCATCTCT SEQ.ID.NO:111	-17	-23.7	72.2	-6.7	0	-4.2
895	GCATTTCCTTAGTCGACACT SEQ.ID.NO:112	-17	-24.8	71.6	-6.9	0	-9.5
899	CTTTGCATTTCCTTAGTCGA SEQ.ID.NO:113	-17	-23.9	69.9	-6.9	0	-5.1
1940	ACAATGTAGAGAAAGTTGTT SEQ.ID.NO:114	-17	-17.5	55.7	0.9	-0.2	-4
46	GAATCCAATTTCGCATTAGG SEQ.ID.NO:115	-16.9	-21.2	61.7	-4.3	0	-3.7
575	ACCACTCTTCAGGCTGCTGG SEQ.ID.NO:116	-16.9	-28.3	80.2	-9.9	-1.4	-6.1
808	GTTTTTGGTAATGCTTCTCC SEQ.ID.NO:117	-16.9	-23.5	70.5	-6.6	0	-3.6
920	ATTCAGCCAACATTCCCATC SEQ.ID.NO:118	-16.9	-25.5	71.4	-8.6	0	-2.4
985	ATCTGCATGCTGCTTCACAT SEQ.ID.NO:119	-16.9	-25.3	73.5	-6.6	-1.8	-9.7
2132	TTTCTGTTGCCATTATGTTT SEQ.ID.NO:120	-16.9	-22.5	68	-5.6	0	-3
214	GTTCACTTTGAGCTATGTTT SEQ.ID.NO:121	-16.8	-22.1	68.2	-4.8	-0.1	-5.1
698	TGATCCTCCCTGCTGACGCG SEQ.ID.NO:122	-16.8	-30.1	78.3	-12	-1.2	-7.4
891	TTCCTTAGTCGACACTCTTG SEQ.ID.NO:123	-16.8	-23.6	69.6	-5.9	0	-9.5
900	TCTTTGCATTTCCTTAGTCG SEQ.ID.NO:124	-16.8	-23.7	70.2	-6.9	0	-5.1
978	TGCTGCTTCACATTTTTTCT SEQ.ID.NO:125	-16.7	-23.3	70	-6.6	0	-6
1145	TTGTTATTTCCTGAGGCATC SEQ.ID.NO:126	-16.7	-23.3	69.9	-6.6	0	-5
1942	ACACAATGTAGAGAAAGTTG SEQ.ID.NO:127	-16.7	-17.1	54.3	0	0	-4.4
1051	GCATGACTTTGTTGTCGAGG SEQ.ID.NO:128	-16.6	-23.9	70	-6	-1.2	-5.2
1725	AGTGGGGTAAACTTGTGGTC SEQ.ID.NO:129	-16.6	-23.5	70.4	-6.9	0	-2.6
43	TCCAATTTCGCATTAGGATA SEQ.ID.NO:130	-16.5	-21.6	63.2	-4.3	-0.6	-4.8
571	CTCTTCAGGCTGCTGGGGGT SEQ.ID.NO:131	-16.5	-30	86.2	-12.5	-0.9	-6.1
676	CATGCGGGGCTTCTTTGTTA SEQ.ID.NO:132	-16.5	-26.2	74.6	-9.1	-0.3	-4.1
877	CTCTTGACACTTTCTTCGCA SEQ.ID.NO:133	-16.5	-24.2	70.7	-7.7	0	-3.6
1656	CGTAATTCAGTCAGGCGACC SEQ.ID.NO:134	-16.5	-25.1	70.3	-7.2	-1.3	-5.1
1797	TATGAGAGAGAAAAAGGAGC SEQ.ID.NO:135	-16.5	-16.9	53.5	0	0	-2.8
223	AGAAGCAGTGTTCACTTTGA SEQ.ID.NO:136	-16.4	-21.9	66.7	-4.8	-0.4	-7.8

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intra-molecular oligo	kcal/mol Inter-molecular oligo
1653	AATTCAGTCAGGCGACCCAG SEQ.ID.NO:137	-16.4	-26.1	72.5	-8.3	-1.3	-5.4
1795	TGAGAGAGAAAAAGGAGCTA SEQ.ID.NO:138	-16.4	-17.8	55.3	-1.3	0	-5.1
49	TCAGAATCCAATTTCGCATT SEQ.ID.NO:139	-16.3	-21.4	62.4	-4.4	-0.4	-3.6
704	CCCCTTTGATCCTCCCTGCT SEQ.ID.NO:140	-16.3	-33	85.7	-16.7	0	-4.3
914	CCAACATTCCCATCTCTTTG SEQ.ID.NO:141	-16.3	-24.9	70	-8.6	0	-2.5
1053	CTGCATGACTTTGTTGTCGA SEQ.ID.NO:142	-16.3	-23.6	69	-6	-1.2	-7.6
1376	ATAGGTCAGAATGCCCAGAC SEQ.ID.NO:143	-16.3	-24.4	70	-6.6	-1.4	-5.8
1781	GAGCTAGACCCCTCCCCTGT SEQ.ID.NO:144	-16.3	-33.2	87.1	-16.9	0	-5.3
42	CCAATTTCGCATTAGGATAA SEQ.ID.NO:145	-16.2	-20.5	59.9	-4.3	0	-3.6
44	ATCCAATTTCGCATTAGGAT SEQ.ID.NO:146	-16.2	-21.9	63.7	-4.3	-1.3	-6.2
441	GGACCTGCCACTTGTTCTGT SEQ.ID.NO:147	-16.2	-28.4	80.2	-11.7	-0.2	-3
604	ACGCCTGAGTTCATATATTC SEQ.ID.NO:148	-16.2	-22.6	66.8	-6.4	0	-3.6
666	TTCTTTGTTACAGGCATCTC SEQ.ID.NO:149	-16.2	-22.9	70.4	-6.7	0	-4.2
695	TCCTCCCTGCTGACGCGCCC SEQ.ID.NO:150	-16.2	-35.3	87.5	-17.8	-1.2	-7.7
839	AGTTGCCCCCGTTTTTACAC SEQ.ID.NO:151	-16.2	-28.3	76.7	-11.4	-0.4	-3.4
999	TCATTCACGGTCTGATCTGC SEQ.ID.NO:152	-16.2	-24.7	72.5	-8.5	0	-4.9
1069	GAGTTCAGTTTTCTCCCTGC SEQ.ID.NO:153	-16.2	-26.9	79.9	-10.7	0	-4.4
662	TTGTTACAGGCATCTCTGCT SEQ.ID.NO:154	-16.1	-25	74.4	-6.7	-2.2	-8.7
896	TGCATTTCCTTAGTCGACAC SEQ.ID.NO:155	-16.1	-23.9	69.5	-6.9	0	-9.5
38	TTTCGCATTAGGATAAGTCG SEQ.ID.NO:156	-16	-20.9	62	-4.3	-0.3	-3.9
663	TTTGTTACAGGCATCTCTGC SEQ.ID.NO:157	-16	-24.2	72.7	-6.7	-1.4	-8.5
703	CCCTTTGATCCTCCCTGCTG SEQ.ID.NO:158	-16	-31	82.3	-15	0	-4.3
897	TTGCATTTCCTTAGTCGACA SEQ.ID.NO:159	-16	-23.8	69.3	-6.9	0	-9.5
1050	CATGACTTTGTTGTCGAGGT SEQ.ID.NO:160	-16	-23.3	69	-6	-1.2	-5.2
1052	TGCATGACTTTGTTGTCGAG SEQ.ID.NO:161	-16	-22.7	67.3	-6	-0.5	-7.6
45	AATCCAATTTCGCATTAGGA SEQ.ID.NO:162	-15.9	-21.2	61.7	-4.3	-0.9	-5.4
664	CTTTGTTACAGGCATCTCTG SEQ.ID.NO:163	-15.9	-23.3	70.2	-6.7	-0.4	-4.4
700	TTTGATCCTCCCTGCTGACG	-15.9	-27.7	75.2	-11.8	0	-4.3

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intramolecular oligo	kcal/mol Intermolecular oligo
	SEQ.ID.NO:164						
806	TTTTGGTAATGCTTCTCCTG SEQ.ID.NO:165	-15.9	-23.1	68.6	-7.2	0	-3.6
1054	CCTGCATGACTTTGTTGTCG SEQ.ID.NO:166	-15.9	-25	71.3	-7.8	-1.2	-7.6
1121	GTTTGTTATATGAATCCATA SEQ.ID.NO:167	-15.9	-18.8	58.6	-1.9	-0.8	-3.4
1123	CTGTTTGTTATATGAATCCA SEQ.ID.NO:168	-15.9	-20	61.1	-4.1	0	-2.4
1686	AGCATCTCAGCGTGGTGATG SEQ.ID.NO:169	-15.9	-25.7	74.4	-8.8	-0.9	-6.2
1721	GGGTAAACTTGTGGTCGTTT SEQ.ID.NO:170	-15.9	-23.3	68.4	-6.9	-0.1	-4.2
1943	AACACAATGTAGAGAAAGTT SEQ.ID.NO:171	-15.9	-16.4	52.5	0	-0.2	-4.4
39	ATTTCGCATTAGGATAAGTC SEQ.ID.NO:172	-15.8	-20.1	61.5	-4.3	0	-3.1
576	TACCACTCTTCAGGCTGCTG SEQ.ID.NO:173	-15.8	-26.8	76.9	-9.9	-1	-6.1
898	TTTGCATTTCCTTAGTCGAC SEQ.ID.NO:174	-15.8	-23.2	68.5	-6.9	0	-8.2
1300	CCCTTTCAGCAAAGCAATCT SEQ.ID.NO:175	-15.8	-24.4	68.4	-7.7	-0.8	-4.7
1650	TCAGTCAGGCGACCCAGGAG SEQ.ID.NO:176	-15.8	-28.5	78.7	-11.3	-1.3	-5.9
48	CAGAATCCAATTTCGCATTA SEQ.ID.NO:177	-15.7	-20.7	60.5	-4.3	-0.4	-3.6
888	CTTAGTCGACACTCTTGACA SEQ.ID.NO:178	-15.7	-22.6	67	-5.3	-1.5	-9.5
892	TTTCCTTAGTCGACACTCTT SEQ.ID.NO:179	-15.7	-23.7	70.1	-7.1	0	-9.5
1049	ATGACTTTGTTGTCGAGGTC SEQ.ID.NO:180	-15.7	-23	69.5	-6	-1.2	-5.2
1673	GGTGATGATTGAATGTCCGT SEQ.ID.NO:181	-15.7	-23.2	67	-7.5	0	-2.8
2047	ATGAGATTTTCCCTAGTTCA SEQ.ID.NO:182	-15.7	-22.9	68.4	-7.2	0	-3.8
37	TTCGCATTAGGATAAGTCGG SEQ.ID.NO:183	-15.6	-22	64.2	-5.6	-0.6	-3.9
440	GACCTGCCACTTGTTCTGTT SEQ.ID.NO:184	-15.6	-27.3	77.9	-11.7	0	-2.3
690	CCTGCTGACGCGCCCATGCG SEQ.ID.NO:185	-15.6	-32.9	80.5	-14.7	-2.6	-9.6
1043	TTGTTGTCGAGGTCACTTGT SEQ.ID.NO:186	-15.6	-24.3	72.9	-8.7	0	-4.9
1926	GTTGTTCTATCTAGCCCAAT SEQ.ID.NO:187	-15.6	-24.4	71.5	-8.8	0	-3.7
212	TCACTTTGAGCTATGTTTCT SEQ.ID.NO:188	-15.5	-22.1	68	-6.6	0	-5.1
1375	TAGGTCAGAATGCCCAGACG SEQ.ID.NO:189	-15.5	-25.2	70.1	-8.2	-1.4	-5.9
837	TTGCCCCCGTTTTTACACTT SEQ.ID.NO:190	-15.4	-28.1	75.3	-12	-0.4	-3.4
851	TATCCATCACACAGTTGCCC SEQ.ID.NO:191	-15.4	-26.8	75	-11.4	0	-3

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intra-molecular oligo	kcal/mol Inter-molecular oligo
1001	CTTCATTCACGGTCTGATCT SEQ.ID.NO:192	-15.4	-23.9	70.6	-8.5	0	-4.9
1305	GCAGACCCTTTCAGCAAAGC SEQ.ID.NO:193	-15.4	-26.4	73.5	-10.1	-0.8	-5
1377	AATAGGTCAGAATGCCCAGA SEQ.ID.NO:194	-15.4	-23.5	67.2	-6.6	-1.4	-4.5
1780	AGCTAGACCCCTCCCCTGTA SEQ.ID.NO:195	-15.4	-32.3	85.3	-16.9	0	-4.3
317	AATGCACTTTCTTTATGGTG SEQ.ID.NO:196	-15.3	-20.7	63	-4.9	-0.1	-5.5
577	GTACCACTCTTCAGGCTGCT SEQ.ID.NO:197	-15.2	-28	80.8	-12.8	0	-6.1
840	CAGTTGCCCCCGTTTTTACA SEQ.ID.NO:198	-15.2	-28.8	77.1	-12.9	-0.4	-2.7
904	CATCTCTTTGCATTTCCTTA SEQ.ID.NO:199	-15.2	-23.3	69.6	-8.1	0	-5.1
1042	TGTTGTCGAGGTCACTTGTC SEQ.ID.NO:100	-15.2	-24.6	74.3	-9.4	0	-4.4
1146	TTTGTTATTTCCTGAGGCAT SEQ.ID.NO:201	-15.2	-23	68.7	-7.8	0	-4
50	CTCAGAATCCAATTTCGCAT SEQ.ID.NO:202	-15.1	-22.2	63.9	-6.4	-0.4	-3.6
697	GATCCTCCCTGCTGACGCGC SEQ.ID.NO:203	-15.1	-31.9	82.5	-15.5	-1.2	-7.7
990	GTCTGATCTGCATGCTGCTT SEQ.ID.NO:204	-15.1	-26.4	77.5	-9.5	-1.8	-9.7
1944	AAACACAATGTAGAGAAAGT SEQ.ID.NO:205	-15.1	-15.6	50.6	0	-0.2	-4.4
47	AGAATCCAATTTCGCATTAG SEQ.ID.NO:206	-15	-20	59.5	-4.3	-0.4	-3.6
572	ACTCTTCAGGCTGCTGGGGG SEQ.ID.NO:207	-15	-29	83	-12.5	-1.4	-6.1
805	TTTGGTAATGCTTCTCCTGA SEQ.ID.NO:208	-15	-23.6	69.6	-8.6	0	-3.6
986	GATCTGCATGCTGCTTCACA SEQ.ID.NO:209	-15	-25.9	74.9	-9.7	-1.1	-9
1048	TGACTTTGTTGTCGAGGTCA SEQ.ID.NO:210	-15	-23.7	70.7	-6.9	-1.8	-6.7
1782	GGAGCTAGACCCCTCCCCTG SEQ.ID.NO:211	-15	-33.2	86.1	-16.9	-1.2	-6.4
2046	TGAGATTTTCCCTAGTTCAA SEQ.ID.NO:212	-15	-22.2	66.2	-7.2	0	-3.8
667	CTTCTTTGTTACAGGCATCT SEQ.ID.NO:213	-14.9	-23.4	70.8	-8.5	0	-4.2
1652	ATTCAGTCAGGCGACCCAGG SEQ.ID.NO:214	-14.9	-28	77.4	-12.1	-0.9	-5.4
1675	GTGGTGATGATTGAATGTCC SEQ.ID.NO:215	-14.9	-22.4	66.6	-7.5	0	-2.8
211	CACTTTGAGCTATGTTTCTA SEQ.ID.NO:216	-14.8	-21.4	65.8	-6.6	0	-5.1
879	CACTCTTGACACTTTCTTCG SEQ.ID.NO:217	-14.8	-22.6	67	-7.8	0	-2.4
1894	GGAAGTTACACATGTAATTA SEQ.ID.NO:218	-14.8	-17.9	56.3	-3.1	0.1	-6.6
40	AATTTCGCATTAGGATAAGT	-14.7	-19	58.1	-4.3	0	-3.9

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intramolecular oligo	kcal/mol Intermolecular oligo
	SEQ.ID.NO:219						
1726	AAGTGGGGTAAACTTGTGGT SEQ.ID.NO:220	-14.7	-22.4	66.4	-7.1	-0.3	-3.6
1779	GCTAGACCCCTCCCCTGTAA SEQ.ID.NO:221	-14.7	-31.6	82.4	-16.9	0	-4.1
1798	ATATGAGAGAGAAAAAGGAG SEQ.ID.NO:222	-14.7	-15.1	49.7	0	0	-1.8
1927	AGTTGTTCTATCTAGCCCAA SEQ.ID.NO:223	-14.7	-24.4	71.8	-9.7	0	-3.7
1928	AAGTTGTTCTATCTAGCCCA SEQ.ID.NO:224	-14.7	-24.4	71.8	-9.7	0	-3.7
225	AGAGAAGCAGTGTTCACTTT SEQ.ID.NO:225	-14.6	-21.9	67.1	-6.6	-0.4	-6.8
688	TGCTGACGCGCCCATGCGGG SEQ.ID.NO:226	-14.6	-32.4	80.3	-13.9	-3.9	-10.9
901	CTCTTTGCATTTCCTTAGTC SEQ.ID.NO:227	-14.6	-23.8	72.2	-9.2	0	-4.8
988	CTGATCTGCATGCTGCTTCA SEQ.ID.NO:228	-14.6	-25.9	75	-9.5	-1.8	-9.7
1378	CAATAGGTCAGAATGCCCAG SEQ.ID.NO:229	-14.6	-23.6	67.1	-8.2	-0.6	-3.7
1984	GGCTTGCCAATTAGAATGCA SEQ.ID.NO:230	-14.6	-24	67.8	-8.3	-1	-7.9
1000	TTCATTCACGGTCTGATCTG SEQ.ID.NO:231	-14.5	-23	68.4	-8.5	0	-4.9
1044	TTTGTTGTCGAGGTCACTTG SEQ.ID.NO:232	-14.5	-23.2	69.7	-8.7	0	-4.9
1153	AATTTTATTTGTTATTTCCT SEQ.ID.NO:233	-14.5	-18	57.3	-3.5	0	-2.3
1674	TGGTGATGATTGAATGTCCG SEQ.ID.NO:234	-14.5	-22	63.8	-7.5	0	-3.5
1895	TGGAAGTTACACATGTAATT SEQ.ID.NO:235	-14.5	-18.2	56.8	-3.1	-0.3	-7.1
1939	CAATGTAGAGAAAGTTGTTC SEQ.ID.NO:236	-14.5	-17.7	56.5	-2.7	-0.1	-2.8
1948	TTTAAAACACAATGTAGAGA SEQ.ID.NO:237	-14.5	-15	49.5	0	-0.2	-5.1
1978	CCAATTAGAATGCAGGATTC SEQ.ID.NO:238	-14.5	-20.5	61	-5	-0.9	-5.5
318	AAATGCACTTTCTTTATGGT SEQ.ID.NO:239	-14.4	-20	61	-5.6	0	-5.5
701	CTTTGATCCTCCCTGCTGAC SEQ.ID.NO:240	-14.3	-27.8	77.4	-13.5	0	-4.3
989	TCTGATCTGCATGCTGCTTC SEQ.ID.NO:241	-14.3	-25.6	75.6	-9.5	-1.8	-9.7
1304	CAGACCCTTTCAGCAAAGCA SEQ.ID.NO:242	-14.3	-25.3	70.4	-10.1	-0.8	-4.7
1590	CACAACTTTTGTAGCACATC SEQ.ID.NO:243	-14.3	-21	63.4	-5.7	-0.9	-6.7
1649	CAGTCAGGCGACCCAGGAGA SEQ.ID.NO:244	-14.3	-28.7	78.3	-13	-1.3	-5.9
1783	AGGAGCTAGACCCCTCCCCT SEQ.ID.NO:245	-14.3	-33.2	86.7	-16.9	-2	-7.6
41	CAATTTCGCATTAGGATAAG SEQ.ID.NO:246	-14.2	-18.5	56.5	-4.3	0	-3.9

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intra-molecular oligo	kcal/mol Inter-molecular oligo
311	CTTTCTTTATGGTGGTCTTC SEQ.ID.NO:247	-14.2	-22.9	71.2	-8.7	0	-1.5
661	TGTTACAGGCATCTCTGCTA SEQ.ID.NO:248	-14.2	-24.6	73.4	-8.2	-2.2	-7.5
693	CTCCCTGCTGACGCGCCCAT SEQ.ID.NO:249	-14.2	-33.6	83.6	-18.1	-1.2	-7.7
876	TCTTGACACTTTCTTCGCAT SEQ.ID.NO:250	-14.2	-23.3	68.7	-9.1	0	-3.6
893	ATTTCCTTAGTCGACACTCT SEQ.ID.NO:251	-14.2	-23.6	69.7	-8.5	0	-9.5
991	GGTCTGATCTGCATGCTGCT SEQ.ID.NO:252	-14.2	-27.5	79.8	-11.5	-1.8	-9.7
1124	TCTGTTTGTTATATGAATCC SEQ.ID.NO:253	-14.2	-19.7	61.3	-5.5	0	-2.4
1672	GTGATGATTGAATGTCCGTA SEQ.ID.NO:254	-14.2	-21.7	63.9	-7.5	0	-2.6
603	CGCCTGAGTTCATATATTCC SEQ.ID.NO:255	-14.1	-24.4	69.9	-10.3	0	-3.6
739	AGAGGCTCTGTCTCCACAAA SEQ.ID.NO:256	-14.1	-24.9	72.1	-9.6	-1.1	-5.1
1251	GGTAGCTTTTTTGTGAATTC SEQ.ID.NO:257	-14.1	-20.9	64.9	-6.8	0	-5.9
1591	ACACAACTTTTGTAGCACAT SEQ.ID.NO:258	-14.1	-20.8	62.5	-5.7	-0.9	-6.7
977	GCTGCTTCACATTTTTTCTC SEQ.ID.NO:259	-14	-23.7	71.9	-9.7	0	-5.2
1227	AGAACCTGTACATGATTGGT SEQ.ID.NO:260	-14	-21.9	64.8	-7.4	-0.1	-6.8
1799	AATATGAGAGAGAAAAAGGA SEQ.ID.NO:261	-14	-14.4	48	0	0	-2.7
1426	AGGTGTTATATATTCATCAG SEQ.ID.NO:262	-13.9	-19.1	61	-5.2	0	-5.2
1687	CAGCATCTCAGCGTGGTGAT SEQ.ID.NO:263	-13.9	-26.4	75.7	-11.5	-0.9	-4.4
1720	GGTAAACTTGTGGTCGTTTA SEQ.ID.NO:264	-13.9	-21.8	65.2	-6.9	-0.9	-5
1947	TTAAAACACAATGTAGAGAA SEQ.ID.NO:265	-13.9	-14.2	47.6	0	0.3	-4.4
2122	CATTATGTTTGCTTTATTGC SEQ.ID.NO:266	-13.9	-20.4	62.9	-6.5	0	-3.6
226	AAGAGAAGCAGTGTTCACTT SEQ.ID.NO:267	-13.8	-21.1	64.4	-6.6	-0.4	-7.5
963	TTTCTCAGTCGCTTAGATTT SEQ.ID.NO:268	-13.8	-22.3	68.1	-8.5	0	-3.1
964	TTTTCTCAGTCGCTTAGATT SEQ.ID.NO:269	-13.8	-22.3	68.1	-8.5	0	-3.1
965	TTTTTCTCAGTCGCTTAGAT SEQ.ID.NO:270	-13.8	-22.3	68.1	-8.5	0	-3.1
1147	ATTTGTTATTTCCTGAGGCA SEQ.ID.NO:271	-13.8	-23	68.7	-9.2	0	-4
1220	GTACATGATTGGTTGCCATT SEQ.ID.NO:272	-13.8	-23.6	69	-9.1	-0.4	-5.9
1221	TGTACATGATTGGTTGCCAT SEQ.ID.NO:273	-13.8	-23.5	68.5	-9	-0.4	-6.6
1223	CCTGTACATGATTGGTTGCC	-13.8	-25.7	73	-11.9	0	-6.1

position	oligo	kcal/ mol total binding	kcal/ mol duplex forma- tion	deg C Tm of Duplex	kcal/ mol target struc- ture	kcal/ mol Intra- mole- cular oligo	kcal/ mol Inter- mole- cular oligo
	SEQ.ID.NO:274						
1250	GTAGCTTTTTGTGAATTCT SEQ.ID.NO:275	-13.8	-20.6	64.3	-6.8	0	-6.9
1648	AGTCAGGCGACCCAGGAGAC SEQ.ID.NO:276	-13.8	-28.2	77.9	-13	-1.3	-6.6
1690	CATCAGCATCTCAGCGTGGT SEQ.ID.NO:277	-13.8	-26.9	77.5	-12.6	-0.1	-4.1
738	GAGGCTCTGTCTCCACAAAC SEQ.ID.NO:278	-13.7	-25.1	72.4	-10.8	-0.3	-4.1
1061	TTTTCTCCCTGCATGACTTT SEQ.ID.NO:279	-13.7	-25.3	72.9	-11.6	0	-4.9
1365	TGCCCAGACGGAAGTTTCTT SEQ.ID.NO:280	-13.7	-26	72.2	-11.4	-0.8	-5
2127	GTTGCCATTATGTTTGCTTT SEQ.ID.NO:281	-13.7	-23.9	70.7	-10.2	0	-3.6
51	GCTCAGAATCCAATTTCGCA SEQ.ID.NO:282	-13.6	-24	67.8	-10.4	0.4	-4
612	GCTGGCATACGCCTGAGTTC SEQ.ID.NO:283	-13.6	-28.1	78.4	-11.6	-2.9	-8.1
1055	CCCTGCATGACTTTGTTGTC SEQ.ID.NO:284	-13.6	-26.2	75.1	-12.1	-0.1	-4.9
1060	TTTCTCCCTGCATGACTTTG SEQ.ID.NO:285	-13.6	-25.2	72.4	-11.6	0	-4.9
1063	AGTTTTCTCCCTGCATGACT SEQ.ID.NO:286	-13.6	-26.3	76	-12.7	0	-4.9
1066	TTCAGTTTTCTCCCTGCATG SEQ.ID.NO:287	-13.6	-25.8	75.2	-12.2	0	-5.7
1366	ATGCCCAGACGGAAGTTTCT SEQ.ID.NO:288	-13.6	-25.9	71.8	-11.4	-0.8	-5
1427	TAGGTGTTATATATTCATCA SEQ.ID.NO:289	-13.6	-18.8	60.1	-5.2	0	-5.2
1647	GTCAGGCGACCCAGGAGACA SEQ.ID.NO:290	-13.6	-28.9	78.6	-14.3	-0.9	-6.5
2123	CCATTATGTTTGCTTTATTG SEQ.ID.NO:291	-13.6	-20.6	62.5	-7	0	-3.6
442	AGGACCTGCCACTTGTTCTG SEQ.ID.NO:292	-13.5	-27.2	76.9	-12.6	-1	-3.6
908	TTCCCATCTCTTTGCATTTC SEQ.ID.NO:293	-13.5	-25.1	73.6	-11.6	0	-5.1
909	ATTCCCATCTCTTTGCATTT SEQ.ID.NO:294	-13.5	-24.7	71.9	-11.2	0	-5.1
1580	GTAGCACATCAAGAAGTGGC SEQ.ID.NO:295	-13.5	-22.8	67.7	-8.4	-0.8	-6.4
1589	ACAACTTTTGTAGCACATCA SEQ.ID.NO:296	-13.5	-21	63.4	-6.6	-0.7	-6.7
1657	CCGTAATTCAGTCAGGCGAC SEQ.ID.NO:297	-13.5	-25.1	70.3	-10.6	-0.9	-4.7
36	TCGCATTAGGATAAGTCGGG SEQ.ID.NO:298	-13.4	-23.1	66.3	-8.9	-0.6	-3.9
213	TTCACTTTGAGCTATGTTTC SEQ.ID.NO:299	-13.4	-21.3	66.3	-7.9	0	-5.1
705	TCCCCTTTGATCCTCCCTGC SEQ.ID.NO:300	-13.4	-32.5	85.7	-19.1	0	-4.3
974	GCTTCACATTTTTTCTCAGT SEQ.ID.NO:301	-13.4	-22.9	70.4	-9.5	0	-2.8

position	oligo	kcal/mol total binding	kcal/mol duplex forma-tion	deg C Tm of Duplex	kcal/mol target struc-ture	kcal/mol Intra-mole-cular oligo	kcal/mol Inter-mole-cular oligo
1034	AGGTCACTTGTCGCAAGTCA SEQ.ID.NO:302	-13.4	-25.2	73.9	-9.8	-2	-10.6
1064	CAGTTTTCTCCCTGCATGAC SEQ.ID.NO:303	-13.4	-26.1	75.1	-12.7	0	-5.4
1364	GCCCAGACGGAAGTTTCTTA SEQ.ID.NO:304	-13.4	-25.7	71.8	-11.4	-0.8	-5.1
1430	ACATAGGTGTTATATATTCA SEQ.ID.NO:305	-13.4	-18.6	59.2	-4.7	-0.2	-5.7
1809	ACATCAGATTAATATGAGAG SEQ.ID.NO:306	-13.4	-16.6	53.7	-3.2	0	-7.4
224	GAGAAGCAGTGTTCACTTTG SEQ.ID.NO:307	-13.3	-21.9	66.7	-7.9	-0.4	-6.8
609	GGCATACGCCTGAGTTCATA SEQ.ID.NO:308	-13.3	-25.8	72.8	-10.3	-2.2	-7.4
809	CGTTTTTGGTAATGCTTCTC SEQ.ID.NO:309	-13.3	-22.3	66.8	-9	0	-3.6
1047	GACTTTGTTGTCGAGGTCAC SEQ.ID.NO:310	-13.3	-23.9	71.5	-9.4	-1.1	-5.6
2045	GAGATTTTCCCTAGTTCAAC SEQ.ID.NO:311	-13.3	-22.4	66.9	-9.1	0	-3.6
2124	GCCATTATGTTTGCTTTATT SEQ.ID.NO:312	-13.3	-22.4	66.9	-9.1	0	-3.6
2126	TTGCCATTATGTTTGCTTTA SEQ.ID.NO:313	-13.3	-22.4	66.8	-9.1	0	-3.6
613	AGCTGGCATACGCCTGAGTT SEQ.ID.NO:314	-13.2	-27.7	77	-11.6	-2.9	-9.3
696	ATCCTCCCTGCTGACGCGCC SEQ.ID.NO:315	-13.2	-33.3	84.4	-18.8	-1.2	-7.7
923	AGCATTCAGCCAACATTCCC SEQ.ID.NO:316	-13.2	-26.9	74.3	-12.7	-0.9	-4.1
1058	TCTCCCTGCATGACTTTGTT SEQ.ID.NO:317	-13.2	-26.3	75.5	-13.1	0	-4.9
1249	TAGCTTTTTTGTGAATTCTA SEQ.ID.NO:318	-13.2	-19.1	60.3	-5.9	0	-6.9
1301	ACCCTTTCAGCAAAGCAATC SEQ.ID.NO:319	-13.2	-23.7	67.1	-9.6	-0.8	-4.7
1579	TAGCACATCAAGAAGTGGCT SEQ.ID.NO:320	-13.2	-22.5	66.4	-8.4	-0.8	-6.4
1945	AAAACACAATGTAGAGAAAG SEQ.ID.NO:321	-13.2	-13.7	46.5	0	-0.2	-4.2
2125	TGCCATTATGTTTGCTTTAT SEQ.ID.NO:322	-13.2	-22.3	66.4	-9.1	0	-3.6
689	CTGCTGACGCGCCCATGCGG SEQ.ID.NO:323	-13.1	-32.1	79.7	-16	-3	-10
694	CCTCCCTGCTGACGCGCCCA SEQ.ID.NO:324	-13.1	-35.6	86.6	-21.2	-1.2	-7.7
1062	GTTTTCTCCCTGCATGACTT SEQ.ID.NO:325	-13.1	-26.4	76	-13.3	0	-4.9
1226	GAACCTGTACATGATTGGTT SEQ.ID.NO:326	-13.1	-22	64.9	-7.6	-1.2	-9
1252	TGGTAGCTTTTTTGTGAATT SEQ.ID.NO:327	-13.1	-20.5	63.3	-7.4	0	-4.6
1679	CAGCGTGGTGATGATTGAAT SEQ.ID.NO:328	-13.1	-22.1	64.2	-9	0	-4.1
1800	TAATATGAGAGAGAAAAAGG	-13.1	-13.5	46.3	0	0	-2.7

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intra-molecular oligo	kcal/mol Inter-molecular oligo
	SEQ.ID.NO:329						
1810	TACATCAGATTAATATGAGA SEQ.ID.NO:330	-13.1	-16.3	53	-3.2	0	-7.4
2120	TTATGTTTGCTTTATTGCCA SEQ.ID.NO:331	-13.1	-22.4	66.8	-9.3	0	-3.6
709	CTCATCCCCTTTGATCCTCC SEQ.ID.NO:332	-13	-29.8	81	-16.8	0	-4.3
913	CAACATTCCCATCTCTTTGC SEQ.ID.NO:333	-13	-24.7	70.5	-11.7	0	-2.6
1039	TGTCGAGGTCACTTGTCGCA SEQ.ID.NO:334	-13	-26.6	76	-12.7	-0.7	-5.7
1057	CTCCCTGCATGACTTTGTTG SEQ.ID.NO:335	-13	-25.9	73.6	-12.9	0	-4.8
1059	TTCTCCCTGCATGACTTTGT SEQ.ID.NO:336	-13	-26.3	75.5	-13.3	0	-4.9
1152	ATTTTATTTGTTATTTCCTG SEQ.ID.NO:337	-13	-18.7	59.2	-5.7	0	-0.7
1224	ACCTGTACATGATTGGTTGC SEQ.ID.NO:338	-13	-23.9	69.9	-10.9	0	-6.2
1247	GCTTTTTTGTGAATTCTACA SEQ.ID.NO:339	-13	-20.3	62.6	-6.8	0	-8.1
1292	GCAAAGCAATCTGGTCTTCA SEQ.ID.NO:340	-13	-23.1	67.7	-10.1	0	-3.7
1298	CTTTCAGCAAAGCAATCTGG SEQ.ID.NO:341	-13	-21.6	63.6	-7.7	-0.7	-4.4
1425	GGTGTTATATATTCATCAGA SEQ.ID.NO:342	-13	-19.7	62.2	-6.7	0	-4.5
1535	TATCCTTTATGTATTGTCTA SEQ.ID.NO:343	-13	-20.1	63	-7.1	0	-1.2
203	GCTATGTTTCTAAGTCTTCT SEQ.ID.NO:344	-12.9	-22	68.7	-9.1	0	-2.8
675	ATGCGGGGCTTCTTTGTTAC SEQ.ID.NO:345	-12.9	-25.7	74.1	-12.2	-0.3	-4.1
710	GCTCATCCCCTTTGATCCTC SEQ.ID.NO:346	-12.9	-29.6	82	-16.7	0	-4.3
994	CACGGTCTGATCTGCATGCT SEQ.ID.NO:347	-12.9	-26.5	74.9	-12.7	0	-9.7
1045	CTTTGTTGTCGAGGTCACTT SEQ.ID.NO:348	-12.9	-24.1	72	-11.2	0	-4.9
1154	AAATTTTATTTGTTATTTCC SEQ.ID.NO:349	-12.9	-16.4	53.4	-3.5	0	-4.3
1303	AGACCCTTTCAGCAAAGCAA SEQ.ID.NO:350	-12.9	-23.9	67.2	-10.1	-0.7	-4.7
1428	ATAGGTGTTATATATTCATC SEQ.ID.NO:351	-12.9	-18.1	58.7	-5.2	0	-4
1592	TACACAACTTTTGTAGCACA SEQ.ID.NO:352	-12.9	-20.5	61.9	-6.6	-0.9	-6.6
1814	GTTATACATCAGATTAATAT SEQ.ID.NO:353	-12.9	-16.1	52.9	-3.2	0	-4.7
1946	TAAAACACAATGTAGAGAAA SEQ.ID.NO:354	-12.9	-13.4	45.9	0	-0.2	-4.4
1949	TTTTAAAACACAATGTAGAG SEQ.ID.NO:355	-12.9	-14.5	48.6	-1	-0.2	-6
2015	GAAGTAACAATCAATTTAAT SEQ.ID.NO:356	-12.9	-13.9	47.2	-0.9	0	-2.9

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intramolecular oligo	kcal/mol Intermolecular oligo
2016	TGAAGTAACAATCAATTTAA SEQ.ID.NO:357	-12.9	-13.9	47.2	-0.9	0	-2.9
2017	TTGAAGTAACAATCAATTTA SEQ.ID.NO:358	-12.9	-14.7	49.1	-0.9	-0.5	-3.8
34	GCATTAGGATAAGTCGGGGA SEQ.ID.NO:359	-12.8	-23.7	68.4	-10.3	-0.3	-3.7
227	TAAGAGAAGCAGTGTTCACT SEQ.ID.NO:360	-12.8	-20.7	63.5	-7.9	0.4	-6.6
702	CCTTTGATCCTCCCTGCTGA SEQ.ID.NO:361	-12.8	-29.6	80.2	-16.8	0	-3.6
852	ATATCCATCACACAGTTGCC SEQ.ID.NO:362	-12.8	-24.8	71.4	-12	0	-3
1120	TTTGTTATATGAATCCATAA SEQ.ID.NO:363	-12.8	-16.9	53.8	-3	-1	-3.6
1248	AGCTTTTTTGTGAATTCTAC SEQ.ID.NO:364	-12.8	-19.6	61.5	-6.8	0	-6.9
1370	CAGAATGCCCAGACGGAAGT SEQ.ID.NO:365	-12.8	-25	68.3	-11.4	-0.6	-4.2
1374	AGGTCAGAATGCCCAGACGG SEQ.ID.NO:366	-12.8	-26.7	73.1	-12.4	-1.4	-5.9
95	GGACTGAGTCTTCCTCTCCA SEQ.ID.NO:367	-12.7	-27.8	80.7	-13.5	-1.6	-6.1
125	GATGGACTTTCAAGGCCCTG SEQ.ID.NO:368	-12.7	-26	72.6	-13.3	0	-7.1
660	GTTACAGGCATCTCTGCTAC SEQ.ID.NO:369	-12.7	-24.8	74.2	-9.9	-2.2	-6.6
836	TGCCCCCGTTTTTACACTTG SEQ.ID.NO:370	-12.7	-28	74.8	-14.6	-0.4	-3.4
903	ATCTCTTTGCATTTCCTTAG SEQ.ID.NO:371	-12.7	-22.6	68.6	-9.9	0	-5.1
1033	GGTCACTTGTCGCAAGTCAC SEQ.ID.NO:372	-12.7	-25.4	74.2	-10.5	-2.2	-10.8
1056	TCCCTGCATGACTTTGTTGT SEQ.ID.NO:373	-12.7	-26.2	75.1	-13.5	0	-4.9
1784	AAGGAGCTAGACCCCTCCCC SEQ.ID.NO:374	-12.7	-31.6	82.3	-16.9	-2	-7.6
2117	TGTTTGCTTTATTGCCAAGA SEQ.ID.NO:375	-12.7	-22.5	66.4	-9.8	0	-3.4
362	GTTCAATGAGATTCATTTTT SEQ.ID.NO:376	-12.6	-18.5	58.7	-4.2	-1.7	-6.2
363	TGTTCAATGAGATTCATTTT SEQ.ID.NO:377	-12.6	-18.4	58.2	-4.2	-1.5	-6
438	CCTGCCACTTGTTCTGTTAA SEQ.ID.NO:378	-12.6	-25.5	72.8	-12.9	0	-3
578	AGTACCACTCTTCAGGCTGC SEQ.ID.NO:379	-12.6	-27.1	79.1	-14.5	0	-5.2
995	TCACGGTCTGATCTGCATGC SEQ.ID.NO:380	-12.6	-26	74.7	-12.7	0	-8.7
1040	TTGTCGAGGTCACTTGTCGC SEQ.ID.NO:381	-12.6	-26	75.3	-12.7	-0.4	-5.4
1228	AAGAACCTGTACATGATTGG SEQ.ID.NO:382	-12.6	-20	59.7	-7.4	0	-6.1
1718	TAAACTTGTGGTCGTTTACT SEQ.ID.NO:383	-12.6	-20.5	62	-7.1	-0.6	-4.7
1792	GAGAGAAAAAGGAGCTAGAC	-12.6	-18	55.9	-5.4	0	-5.1

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intra-molecular oligo	kcal/mol Inter-molecular oligo
	SEQ.ID.NO:384						
2118	ATGTTTGCTTTATTGCCAAG SEQ.ID.NO:385	-12.6	-21.9	65	-9.3	0	-3.6
309	TTCTTTATGGTGGTCTTCAA SEQ.ID.NO:386	-12.5	-21.9	67.4	-9.4	0	-3.3
494	ACTGAACATTGCTGTATTGC SEQ.ID.NO:387	-12.5	-21.5	64.3	-9	0	-3.9
574	CCACTCTTCAGGCTGCTGGG SEQ.ID.NO:388	-12.5	-29.3	82.2	-15.3	-1.4	-6.1
611	CTGGCATACGCCTGAGTTCA SEQ.ID.NO:389	-12.5	-27	75.2	-11.6	-2.9	-7.9
736	GGCTCTGTCTCCACAAACAA SEQ.ID.NO:390	-12.5	-24.5	69.6	-12	0.1	-3.8
1041	GTTGTCGAGGTCACTTGTCG SEQ.ID.NO:391	-12.5	-25.4	74.3	-12.9	0.4	-4.9
1811	ATACATCAGATTAATATGAG SEQ.ID.NO:392	-12.5	-15.7	51.7	-3.2	0	-6.9
2018	ATTGAAGTAACAATCAATTT SEQ.ID.NO:393	-12.5	-15	49.6	-0.9	-1.4	-5.5
364	ATGTTCAATGAGATTCATTT SEQ.ID.NO:394	-12.4	-18.3	57.9	-4.2	-1.7	-6.2
668	GCTTCTTTGTTACAGGCATC SEQ.ID.NO:395	-12.4	-24.3	73.3	-11.9	0	-4.2
1112	ATGAATCCATAATAAAATGT SEQ.ID.NO:396	-12.4	-14.8	48.5	-2.4	0	-2.8
1534	ATCCTTTATGTATTGTCTAT SEQ.ID.NO:397	-12.4	-20.4	63.6	-8	0	-0.9
1689	ATCAGCATCTCAGCGTGGTG SEQ.ID.NO:398	-12.4	-26.2	76.2	-12.6	-1.1	-4.1
1790	GAGAAAAAGGAGCTAGACCC SEQ.ID.NO:399	-12.4	-21.4	61.7	-9	0	-5.8
1896	GTGGAAGTTACACATGTAAT SEQ.ID.NO:400	-12.4	-19.3	59.5	-6	-0.8	-7.1
1899	GTTGTGGAAGTTACACATGT SEQ.ID.NO:401	-12.4	-21.6	65.7	-7.5	-1.7	-6.1
2014	AAGTAACAATCAATTTAATT SEQ.ID.NO:402	-12.4	-13.4	46.3	-0.9	0	-2.9
2044	AGATTTTCCCTAGTTCAACA SEQ.ID.NO:403	-12.4	-22.5	66.7	-10.1	0	-3.6
93	ACTGAGTCTTCCTCTCCAGA SEQ.ID.NO:404	-12.3	-26.6	78.3	-13	-1.2	-4.9
96	TGGACTGAGTCTTCCTCTCC SEQ.ID.NO:405	-12.3	-27.1	79.4	-13.5	-1.2	-6.9
126	AGATGGACTTTCAAGGCCCT SEQ.ID.NO:406	-12.3	-26	73	-13.7	0	-7.1
142	GATTGTTTTGGGTCAGAGAT SEQ.ID.NO:407	-12.3	-22.1	67.7	-9.8	0	-2.7
602	GCCTGAGTTCATATATTCCA SEQ.ID.NO:408	-12.3	-24.3	71	-12	0	-3.6
1002	TCTTCATTCACGGTCTGATC SEQ.ID.NO:409	-12.3	-23.4	70.2	-11.1	0	-3.9
1253	CTGGTAGCTTTTTTGTGAAT SEQ.ID.NO:410	-12.3	-21.3	64.9	-9	0	-4.3
1306	CGCAGACCCTTTCAGCAAAG SEQ.ID.NO:411	-12.3	-25.4	69.4	-12	-1	-4.8

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intra-molecular oligo	kcal/mol Inter-molecular oligo
1371	TCAGAATGCCCAGACGGAAG SEQ.ID.NO:412	-12.3	-24.2	66.7	-11.4	-0.1	-3.5
1670	GATGATTGAATGTCCGTAAT SEQ.ID.NO:413	-12.3	-19.8	59	-7.5	0	-2.6
1671	TGATGATTGAATGTCCGTAA SEQ.ID.NO:414	-12.3	-19.8	58.9	-7.5	0	-2.6
1794	GAGAGAGAAAAAGGAGCTAG SEQ.ID.NO:415	-12.3	-17.8	55.6	-5.5	0	-5.1
1964	GGATTCCCTGGAGCCTTTTA SEQ.ID.NO:416	-12.3	-27.7	77.2	-15.4	0	-4.6
1967	GCAGGATTCCCTGGAGCCTT SEQ.ID.NO:417	-12.3	-30.3	82.8	-15	-3	-9.1
2119	TATGTTTGCTTTATTGCCAA SEQ.ID.NO:418	-12.3	-21.6	64.2	-9.3	0	-3.6
2131	TTCTGTTGCCATTATGTTTG SEQ.ID.NO:419	-12.3	-22.4	67.4	-10.1	0	-3
439	ACCTGCCACTTGTTCTGTTA SEQ.ID.NO:420	-12.2	-26.4	75.9	-14.2	0	-3
485	TGCTGTATTGCGAGTATGGT SEQ.ID.NO:421	-12.2	-24.2	70.9	-11.1	-0.7	-4.1
804	TTGGTAATGCTTCTCCTGAA SEQ.ID.NO:422	-12.2	-22.8	66.9	-10.6	0	-3.2
975	TGCTTCACATTTTTTCTCAG SEQ.ID.NO:423	-12.2	-21.7	66.7	-9.5	0	-3.6
993	ACGGTCTGATCTGCATGCTG SEQ.ID.NO:424	-12.2	-25.8	73.6	-12.7	0	-9.7
1368	GAATGCCCAGACGGAAGTTT SEQ.ID.NO:425	-12.2	-24.5	67.6	-11.4	-0.8	-4.4
1578	AGCACATCAAGAAGTGGCTC SEQ.ID.NO:426	-12.2	-23.2	68.5	-10.1	-0.8	-6.4
1588	CAACTTTTGTAGCACATCAA SEQ.ID.NO:427	-12.2	-20.1	60.7	-7.4	-0.1	-5.6
1668	TGATTGAATGTCCGTAATTC SEQ.ID.NO:428	-12.2	-19.7	59.4	-7.5	0.4	-5.2
1812	TATACATCAGATTAATATGA SEQ.ID.NO:429	-12.2	-15.4	51	-3.2	0	-7.2
1950	CTTTTAAAACACAATGTAGA SEQ.ID.NO:430	-12.2	-15.4	50.3	-2.7	-0.2	-6.2
1968	TGCAGGATTCCCTGGAGCCT SEQ.ID.NO:431	-12.2	-30.2	82.1	-15	-3	-9.1
118	TTTCAAGGCCCTGGGAGGAT SEQ.ID.NO:432	-12.1	-27.3	75.6	-14.4	-0.6	-8.3
210	ACTTTGAGCTATGTTTCTAA SEQ.ID.NO:433	-12.1	-20	62.2	-7.9	0	-5.1
310	TTTCTTTATGGTGGTCTTCA SEQ.ID.NO:434	-12.1	-22.7	70.3	-10.6	0	-3.1
671	GGGGCTTCTTTGTTACAGGC SEQ.ID.NO:435	-12.1	-26.8	78.8	-14.7	0	-3.7
810	GCGTTTTTGGTAATGCTTCT SEQ.ID.NO:436	-12.1	-23.7	69.6	-10.9	-0.5	-3.9
1369	AGAATGCCCAGACGGAAGTT SEQ.ID.NO:437	-12.1	-24.4	67.5	-11.4	-0.8	-3.9
1482	GCATACTCCTCTTGAGTCAT SEQ.ID.NO:438	-12.1	-24.9	73.9	-11.1	-1.7	-6.8
1581	TGTAGCACATCAAGAAGTGG	-12.1	-21	63.3	-8.4	-0.1	-5.7

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intra-molecular oligo	kcal/mol Inter-molecular oligo
	SEQ.ID.NO:439						
1719	GTAAACTTGTGGTCGTTTAC SEQ.ID.NO:440	-12.1	-20.8	63.2	-6.9	-1.8	-6
1815	AGTTATACATCAGATTAATA SEQ.ID.NO:441	-12.1	-16.1	53	-4	0	-4.7
987	TGATCTGCATGCTGCTTCAC SEQ.ID.NO:442	-12	-25.2	73.6	-11.4	-1.8	-9.7
997	ATTCACGGTCTGATCTGCAT SEQ.ID.NO:443	-12	-24.3	70.8	-12.3	0	-4.9
1213	ATTGGTTGCCATTTCCGTCA SEQ.ID.NO:444	-12	-26.8	75.1	-14.1	-0.4	-4.6
1225	AACCTGTACATGATTGGTTG SEQ.ID.NO:445	-12	-21.4	63.5	-8.5	-0.8	-8.2
1276	TTCATGGTCCAAAGTCTGAA SEQ.ID.NO:446	-12	-21.7	64.3	-9.7	0	-5
1277	CTTCATGGTCCAAAGTCTGA SEQ.ID.NO:447	-12	-23.3	68.5	-11.3	0	-5
1295	TCAGCAAAGCAATCTGGTCT SEQ.ID.NO:448	-12	-23	67.6	-10.1	-0.7	-4.4
1312	TTCAACCGCAGACCCTTTCA SEQ.ID.NO:449	-12	-27	72.9	-15	0	-3.6
1367	AATGCCCAGACGGAAGTTTC SEQ.ID.NO:450	-12	-24.3	67.8	-11.4	-0.8	-4.4
1536	CTATCCTTTATGTATTGTCT SEQ.ID.NO:451	-12	-21.3	65.7	-9.3	0	-1.2
1801	TTAATATGAGAGAGAAAAAG SEQ.ID.NO:452	-12	-12.4	44.3	0	0	-2.7
360	TCAATGAGATTCATTTTTGA SEQ.ID.NO:453	-11.9	-17.8	56.5	-4.2	-1.7	-7.2
674	TGCGGGGCTTCTTTGTTACA SEQ.ID.NO:454	-11.9	-26.4	75.2	-13.9	-0.3	-4.1
910	CATTCCCATCTCTTTGCATT SEQ.ID.NO:455	-11.9	-25.3	72.7	-13.4	0	-5.1
1148	TATTTGTTATTTCCTGAGGC SEQ.ID.NO:456	-11.9	-22	66.8	-10.1	0	-3.6
1429	CATAGGTGTTATATATTCAT SEQ.ID.NO:457	-11.9	-18.4	58.6	-6.5	0	-3.9
1553	GCTTCTCTACTGCCTCTCTA SEQ.ID.NO:458	-11.9	-27.2	80.5	-15.3	0	-3.1
1665	TTGAATGTCCGTAATTCAGT SEQ.ID.NO:459	-11.9	-21	62.6	-7.5	-1.6	-6.4
1953	AGCCTTTTAAAACACAATGT SEQ.ID.NO:460	-11.9	-18.9	56.9	-7	0	-6.2
167	TTCTACGATGTCTTCTACCT SEQ.ID.NO:461	-11.8	-23.4	69.2	-11.6	0	-3
922	GCATTCAGCCAACATTCCCA SEQ.ID.NO:462	-11.8	-27.6	75.1	-15.3	-0.1	-3.5
1222	CTGTACATGATTGGTTGCCA SEQ.ID.NO:463	-11.8	-24.4	70.5	-12.1	-0.2	-6.5
1297	TTTCAGCAAAGCAATCTGGT SEQ.ID.NO:464	-11.8	-21.9	64.8	-9.6	-0.2	-4.1
1373	GGTCAGAATGCCCAGACGGA SEQ.ID.NO:465	-11.8	-27.3	74.1	-14.2	-1.2	-5.2
1669	ATGATTGAATGTCCGTAATT SEQ.ID.NO:466	-11.8	-19.3	58.1	-7.5	0	-3

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intra-molecular oligo	kcal/mol Inter-molecular oligo
98	TCTGGACTGAGTCTTCCTCT SEQ.ID.NO:467	-11.7	-26	77.7	-13	-1.2	-6.9
308	TCTTTATGGTGGTCTTCAAA SEQ.ID.NO:468	-11.7	-21.1	64.6	-9.4	0	-3.3
966	TTTTTTCTCAGTCGCTTAGA SEQ.ID.NO:469	-11.7	-22.4	68.5	-10.7	0	-3.1
1065	TCAGTTTTCTCCCTGCATGA SEQ.ID.NO:470	-11.7	-26.3	76.2	-14.6	0	-5.7
1254	CCTGGTAGCTTTTTTGTGAA SEQ.ID.NO:471	-11.7	-23.3	68.8	-11.6	0	-4.6
1294	CAGCAAAGCAATCTGGTCTT SEQ.ID.NO:472	-11.7	-22.7	66.4	-10.1	-0.7	-4.4
1379	CCAATAGGTCAGAATGCCCA SEQ.ID.NO:473	-11.7	-25.6	70.3	-12.4	-1.4	-4.5
1813	TTATACATCAGATTAATATG SEQ.ID.NO:474	-11.7	-14.9	50	-3.2	0	-5.9
1938	AATGTAGAGAAAGTTGTTCT SEQ.ID.NO:475	-11.7	-17.9	57.2	-4.9	-1.2	-3.9
2130	TCTGTTGCCATTATGTTTGC SEQ.ID.NO:476	-11.7	-24.1	71.5	-12.4	0	-3
127	GAGATGGACTTTCAAGGCCC SEQ.ID.NO:477	-11.6	-25.7	72.4	-14.1	0	-7.1
737	AGGCTCTGTCTCCACAAACA SEQ.ID.NO:478	-11.6	-25.2	72.2	-13.1	-0.2	-3.8
835	GCCCCCGTTTTTACACTTGT SEQ.ID.NO:479	-11.6	-29.2	78.2	-16.9	-0.4	-3.1
992	CGGTCTGATCTGCATGCTGC SEQ.ID.NO:480	-11.6	-27.4	77.4	-14.6	-1	-9.7
1014	CGACCTTCACTGTCTTCATT SEQ.ID.NO:481	-11.6	-24.6	71.1	-12.3	-0.5	-3.7
1565	GTGGCTCCTGAAGCTTCTCT SEQ.ID.NO:482	-11.6	-27.7	80.3	-14	-2.1	-10.8
1583	TTTGTAGCACATCAAGAAGT SEQ.ID.NO:483	-11.6	-20	61.5	-8.4	0	-5.1
1793	AGAGAGAAAAAGGAGCTAGA SEQ.ID.NO:484	-11.6	-17.8	55.6	-6.2	0	-5.1
1925	TTGTTCTATCTAGCCCAATA SEQ.ID.NO:485	-11.6	-22.9	67.6	-11.3	0	-3.7
446	CCAGAGGACCTGCCACTTGT SEQ.ID.NO:486	-11.5	-29.1	79.3	-16.7	-0.7	-4.6
1275	TCATGGTCCAAAGTCTGAAA SEQ.ID.NO:487	-11.5	-20.9	61.9	-9.4	0	-5
1593	TTACACAACTTTTGTAGCAC SEQ.ID.NO:488	-11.5	-19.9	61	-7.4	-0.9	-5.8
1683	ATCTCAGCGTGGTGATGATT SEQ.ID.NO:489	-11.5	-23.9	70.3	-11.4	-0.9	-5.2
1691	ACATCAGCATCTCAGCGTGG SEQ.ID.NO:490	-11.5	-25.9	74.5	-13.4	-0.9	-4.2
1759	TCCCCATCACTGCACGTCCC SEQ.ID.NO:491	-11.5	-32.4	83.8	-20.9	0	-4.8
1778	CTAGACCCCTCCCCTGTAAT SEQ.ID.NO:492	-11.5	-29.8	78.3	-18.3	0	-3
1913	GCCCAATATTTACAGTTGTG SEQ.ID.NO:493	-11.5	-22.8	66.4	-11.3	0	-4.1
2116	GTTTGCTTTATTGCCAAGAT	-11.5	-22.5	66.5	-11	0	-3.6

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intra-molecular oligo	kcal/mol Inter-molecular oligo
	SEQ.ID.NO:494						
92	CTGAGTCTTCCTCTCCAGAT SEQ.ID.NO:495	-11.4	-26.4	77.6	-13.7	-1.2	-4.3
361	TTCAATGAGATTCATTTTTG SEQ.ID.NO:496	-11.4	-17.3	55.5	-4.2	-1.7	-6.2
1293	AGCAAAGCAATCTGGTCTTC SEQ.ID.NO:497	-11.4	-22.4	66.8	-10.1	-0.7	-4.4
1667	GATTGAATGTCCGTAATTCA SEQ.ID.NO:498	-11.4	-20.4	60.6	-7.5	-1.4	-6
1806	TCAGATTAATATGAGAGAGA SEQ.ID.NO:499	-11.4	-16.9	54.6	-5.5	0	-6.5
2013	AGTAACAATCAATTTAATTA SEQ.ID.NO:500	-11.4	-13.8	47.3	-2.4	0	-3.7
99	TTCTGGACTGAGTCTTCCTC SEQ.ID.NO:501	-11.3	-25.2	75.9	-13	-0.7	-6.9
141	ATTGTTTTGGGTCAGAGATG SEQ.ID.NO:502	-11.3	-21.5	66.1	-9.6	-0.3	-3.5
573	CACTCTTCAGGCTGCTGGGG SEQ.ID.NO:503	-11.3	-28.5	81.3	-15.7	-1.4	-6.1
614	CAGCTGGCATACGCCTGAGT SEQ.ID.NO:504	-11.3	-28.3	77.7	-14.8	-2.2	-9.9
1119	TTGTTATATGAATCCATAAT SEQ.ID.NO:505	-11.3	-16.8	53.5	-4.4	-1	-3.6
1212	TTGGTTGCCATTTCCGTCAA SEQ.ID.NO:506	-11.3	-26.1	72.7	-14.1	-0.4	-4.6
1954	GAGCCTTTTAAAACACAATG SEQ.ID.NO:507	-11.3	-18.3	55.4	-7	0	-6
2121	ATTATGTTTGCTTTATTGCC SEQ.ID.NO:508	-11.3	-21.7	65.5	-10.4	0	-3.6
117	TTCAAGGCCCTGGGAGGATT SEQ.ID.NO:509	-11.2	-27.3	75.6	-15.3	-0.6	-8.3
437	CTGCCACTTGTTCTGTTAAA SEQ.ID.NO:510	-11.2	-22.8	66.9	-11.6	0	-3
610	TGGCATACGCCTGAGTTCAT SEQ.ID.NO:511	-11.2	-26.1	73.2	-12	-2.9	-7.9
976	CTGCTTCACATTTTTTCTCA SEQ.ID.NO:512	-11.2	-22.6	68.5	-11.4	0	-3.6
1046	ACTTTGTTGTCGAGGTCACT SEQ.ID.NO:513	-11.2	-24.2	72.2	-13	0	-4.9
1070	TGAGTTCAGTTTTCTCCCTG SEQ.ID.NO:514	-11.2	-25.1	74.9	-13.3	-0.3	-4.3
1216	ATGATTGGTTGCCATTTCCG SEQ.ID.NO:515	-11.2	-25.1	70.2	-13.2	-0.4	-4.6
1219	TACATGATTGGTTGCCATTT SEQ.ID.NO:516	-11.2	-22.5	66.1	-10.6	-0.4	-5.9
1255	TCCTGGTAGCTTTTTTGTGA SEQ.ID.NO:517	-11.2	-24.4	72.9	-13.2	0	-4.6
1291	CAAAGCAATCTGGTCTTCAT SEQ.ID.NO:518	-11.2	-21.3	63.5	-10.1	0	-4.1
1431	AACATAGGTGTTATATATTC SEQ.ID.NO:519	-11.2	-17.2	55.8	-4.7	-1.2	-7
1554	AGCTTCTCTACTGCCTCTCT SEQ.ID.NO:520	-11.2	-27.5	81.5	-16.3	0	-4.3
1586	ACTTTTGTAGCACATCAAGA SEQ.ID.NO:521	-11.2	-20.7	63.1	-8.4	-1	-6.9

position	oligo	kcal/ mol total binding	kcal/ mol duplex forma- tion	deg C Tm of Duplex	kcal/ mol target struc- ture	kcal/ mol Intra- mole- cular oligo	kcal/ mol Inter- mole- cular oligo
1680	TCAGCGTGGTGATGATTGAA SEQ.ID.NO:522	-11.2	-22.5	65.7	-10.4	-0.7	-4.6
1684	CATCTCAGCGTGGTGATGAT SEQ.ID.NO:523	-11.2	-24.5	71.1	-12.3	-0.9	-5.6
1900	AGTTGTGGAAGTTACACATG SEQ.ID.NO:524	-11.2	-20.4	62.7	-7.5	-1.7	-5.9
67	CGATTTTGCTACAAATGCTC SEQ.ID.NO:525	-11.1	-20.7	61	-8.8	-0.6	-5.2
486	TTGCTGTATTGCGAGTATGG SEQ.ID.NO:526	-11.1	-23.1	67.9	-11.1	-0.7	-4.1
672	CGGGGCTTCTTTGTTACAGG SEQ.ID.NO:527	-11.1	-25.8	73.9	-14.7	0	-3.7
1215	TGATTGGTTGCCATTTCCGT SEQ.ID.NO:528	-11.1	-26.3	73.5	-14.5	-0.4	-4.6
1543	TGCCTCTCTATCCTTTATGT SEQ.ID.NO:529	-11.1	-25.4	74.7	-14.3	0	-3
1688	TCAGCATCTCAGCGTGGTGA SEQ.ID.NO:530	-11.1	-26.8	77.6	-13.9	-1.8	-4.2
1716	AACTTGTGGTCGTTTACTCT SEQ.ID.NO:531	-11.1	-22.8	68.3	-11.7	0	-3
1952	GCCTTTTAAAACACAATGTA SEQ.ID.NO:532	-11.1	-18.6	56.2	-7	-0.2	-6.2
33	CATTAGGATAAGTCGGGGAG SEQ.ID.NO:533	-11	-21.9	64.5	-10.3	-0.3	-3
35	CGCATTAGGATAAGTCGGGG SEQ.ID.NO:534	-11	-23.9	67.3	-12.3	-0.3	-3.9
64	TTTTGCTACAAATGCTCAGA SEQ.ID.NO:535	-11	-20.6	61.9	-8.8	-0.6	-5.2
66	GATTTTGCTACAAATGCTCA SEQ.ID.NO:536	-11	-20.6	61.7	-8.8	-0.6	-5.2
140	TTGTTTTGGGTCAGAGATGG SEQ.ID.NO:537	-11	-22.7	68.9	-10.8	-0.7	-3.6
1660	TGTCCGTAATTCAGTCAGGC SEQ.ID.NO:538	-11	-25.1	73.2	-14.1	0	-3.4
1717	AAACTTGTGGTCGTTTACTC SEQ.ID.NO:539	-11	-21.2	64	-10.2	0	-4.1
601	CCTGAGTTCATATATTCCAG SEQ.ID.NO:540	-10.9	-22.5	66.9	-11.6	0	-3.6
670	GGGCTTCTTTGTTACAGGCA SEQ.ID.NO:541	-10.9	-26.3	77.1	-14.7	-0.4	-4.2
970	CACATTTTTTCTCAGTCGCT SEQ.ID.NO:542	-10.9	-23.6	70.1	-12.7	0	-3.1
1585	CTTTTGTAGCACATCAAGAA SEQ.ID.NO:543	-10.9	-19.8	60.5	-8.4	-0.1	-5.4
1595	TCTTACACAACTTTTGTAGC SEQ.ID.NO:544	-10.9	-20.3	62.7	-8.4	-0.9	-4.4
1791	AGAGAAAAAGGAGCTAGACC SEQ.ID.NO:545	-10.9	-19.4	58.3	-8.5	0	-5.4
1841	AACTGGGTACAAGTGAAATA SEQ.ID.NO:546	-10.9	-18	55.6	-7.1	0	-6
1912	CCCAATATTTACAGTTGTGG SEQ.ID.NO:547	-10.9	-22.2	64.8	-11.3	0	-4.1
1955	GGAGCCTTTTAAAACACAAT SEQ.ID.NO:548	-10.9	-19.5	57.8	-8.6	0	-6.2
2128	TGTTGCCATTATGTTTGCTT	-10.9	-23.8	70.2	-12.9	0	-3.6

position	oligo	kcal/ mol total binding	kcal/ mol duplex formation	deg C Tm of Duplex	kcal/ mol target structure	kcal/ mol Intra-molecular oligo	kcal/ mol Inter-molecular oligo
	SEQ.ID.NO:549						
100	ATTCTGGACTGAGTCTTCCT SEQ.ID.NO:550	-10.8	-24.8	74	-13	-0.9	-6.2
112	GGCCCTGGGAGGATTCTGGA SEQ.ID.NO:551	-10.8	-29.9	82	-18.3	-0.6	-8.3
735	GCTCTGTCTCCACAAACAAC SEQ.ID.NO:552	-10.8	-23.5	67.7	-12.2	-0.1	-2.9
875	CTTGACACTTTCTTCGCATG SEQ.ID.NO:553	-10.8	-22.9	67	-12.1	0	-4.5
962	TTCTCAGTCGCTTAGATTTA SEQ.ID.NO:554	-10.8	-21.9	67.1	-11.1	0	-3.1
1261	CTGAAATCCTGGTAGCTTTT SEQ.ID.NO:555	-10.8	-22.5	66.2	-11.7	0	-4.7
1582	TTGTAGCACATCAAGAAGTG SEQ.ID.NO:556	-10.8	-19.9	61	-8.4	-0.4	-5.7
1646	TCAGGCGACCCAGGAGACAG SEQ.ID.NO:557	-10.8	-27.7	75.5	-15.9	-0.9	-5.4
1682	TCTCAGCGTGGTGATGATTG SEQ.ID.NO:558	-10.8	-23.9	70.1	-12.1	-0.9	-4.8
1816	AAGTTATACATCAGATTAAT SEQ.ID.NO:559	-10.8	-15.7	51.8	-4.9	0	-4.6
1965	AGGATTCCCTGGAGCCTTTT SEQ.ID.NO:560	-10.8	-28	78.1	-16.3	-0.7	-6
1977	CAATTAGAATGCAGGATTCC SEQ.ID.NO:561	-10.8	-20.5	61	-8.3	-1.3	-5.8
119	CTTTCAAGGCCCTGGGAGGA SEQ.ID.NO:562	-10.7	-28.2	77.6	-16.7	-0.6	-8.3
164	TACGATGTCTTCTACCTCCT SEQ.ID.NO:563	-10.7	-25.3	72.5	-14.6	0	-3.5
570	TCTTCAGGCTGCTGGGGGTA SEQ.ID.NO:564	-10.7	-28.8	83.5	-16.6	-1.4	-6.1
812	CAGCGTTTTTGGTAATGCTT SEQ.ID.NO:565	-10.7	-23.1	67.4	-10.9	-1.4	-5.5
1111	TGAATCCATAATAAAATGTA SEQ.ID.NO:566	-10.7	-14.5	48	-3.8	0	-2.8
1211	TGGTTGCCATTTCCGTCAAA SEQ.ID.NO:567	-10.7	-25.3	70.1	-14.1	-0.2	-4.2
1229	CAAGAACCTGTACATGATTG SEQ.ID.NO:568	-10.7	-19.5	58.5	-8.8	0	-6.1
1264	AGTCTGAAATCCTGGTAGCT SEQ.ID.NO:569	-10.7	-23.8	70.2	-13.1	0	-4.6
1311	TCAACCGCAGACCCTTTCAG SEQ.ID.NO:570	-10.7	-26.9	72.8	-16.2	0	-3.6
1394	TTCGAATTCTTTCTTCCAAT SEQ.ID.NO:571	-10.7	-20.6	61.6	-9.1	-0.6	-6.4
1566	AGTGGCTCCTGAAGCTTCTC SEQ.ID.NO:572	-10.7	-26.8	78.6	-14	-2.1	-10.8
1616	GAGGATTTTCAGGCTGGTGA SEQ.ID.NO:573	-10.7	-24.7	73.2	-14	0	-3.9
1666	ATTGAATGTCCGTAATTCAG SEQ.ID.NO:574	-10.7	-19.8	59.6	-7.5	-1.6	-6.4
1714	CTTGTGGTCGTTTACTCTCC SEQ.ID.NO:575	-10.7	-25.7	75.7	-15	0	-3.3
1789	AGAAAAAGGAGCTAGACCCC SEQ.ID.NO:576	-10.7	-22.8	64	-12.1	0	-5.8

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intramolecular oligo	kcal/mol Intermolecular oligo
1931	AGAAAGTTGTTCTATCTAGC SEQ.ID.NO:577	-10.7	-19.6	62	-7.9	-0.9	-5.4
307	CTTTATGGTGGTCTTCAAAA SEQ.ID.NO:578	-10.6	-20	61	-9.4	0	-2.9
1071	GTGAGTTCAGTTTTCTCCCT SEQ.ID.NO:579	-10.6	-26.3	78.9	-15.1	-0.3	-3.6
1307	CCGCAGACCCTTTCAGCAAA SEQ.ID.NO:580	-10.6	-27.4	72.5	-15.7	-1	-4.1
1386	CTTTCTTCCAATAGGTCAGA SEQ.ID.NO:581	-10.6	-22.7	68.2	-11.4	-0.5	-3.8
1388	TTCTTTCTTCCAATAGGTCA SEQ.ID.NO:582	-10.6	-22.6	68.5	-11.4	-0.3	-3.6
1395	TTTCGAATTCTTTCTTCCAA SEQ.ID.NO:583	-10.6	-20.7	61.9	-9.3	-0.6	-6.7
1483	AGCATACTCCTCTTGAGTCA SEQ.ID.NO:584	-10.6	-24.9	74.2	-12.8	-1.4	-7.5
1727	GAAGTGGGGTAAACTTGTGG SEQ.ID.NO:585	-10.6	-21.8	64.5	-10.2	-0.9	-4.1
1802	ATTAATATGAGAGAGAAAAA SEQ.ID.NO:586	-10.6	-12.4	44.2	-1.8	0	-3.8
1937	ATGTAGAGAAAGTTGTTCTA SEQ.ID.NO:587	-10.6	-18.3	58.6	-6.2	-1.4	-4.6
32	ATTAGGATAAGTCGGGGAGA SEQ.ID.NO:588	-10.5	-21.8	64.7	-11.3	0.1	-3
101	GATTCTGGACTGAGTCTTCC SEQ.ID.NO:589	-10.5	-24.5	73.4	-13	-0.9	-5.9
568	TTCAGGCTGCTGGGGGTAGA SEQ.ID.NO:590	-10.5	-28.1	81.2	-16.1	-1.4	-5.4
811	AGCGTTTTTGGTAATGCTTC SEQ.ID.NO:591	-10.5	-22.8	67.8	-10.9	-1.3	-5.3
894	CATTTCCTTAGTCGACACTC SEQ.ID.NO:592	-10.5	-23.4	68.9	-12	0	-9.5
924	AAGCATTCAGCCAACATTCC SEQ.ID.NO:593	-10.5	-24.2	68.5	-12.7	-0.9	-4.1
1210	GGTTGCCATTTCCGTCAAAA SEQ.ID.NO:594	-10.5	-24.6	68.1	-14.1	0	-3.1
1313	CTTCAACCGCAGACCCTTTC SEQ.ID.NO:595	-10.5	-27.2	73.6	-16.7	0	-3.6
1387	TCTTTCTTCCAATAGGTCAG SEQ.ID.NO:596	-10.5	-22.5	68.4	-11.4	-0.3	-3.6
1396	ATTTCGAATTCTTTCTTCCA SEQ.ID.NO:597	-10.5	-21.4	64	-10.4	-0.1	-6.7
1584	TTTTGTAGCACATCAAGAAG SEQ.ID.NO:598	-10.5	-18.9	58.7	-8.4	0	-5.1
1603	CTGGTGAATCTTACACAACT SEQ.ID.NO:599	-10.5	-20.5	61.5	-8.4	-1.6	-4.8
1763	GTAATCCCCATCACTGCACG SEQ.ID.NO:600	-10.5	-27	72.7	-16.5	0	-4.8
1985	GGGCTTGCCAATTAGAATGC SEQ.ID.NO:601	-10.5	-24.5	69.2	-12.2	-1.8	-8.5
2061	GTAAGATGAGCAAAATGAGA SEQ.ID.NO:602	-10.5	-17	53.5	-6.5	0	-4.1
65	ATTTTGCTACAAATGCTCAG SEQ.ID.NO:603	-10.4	-20	60.6	-8.8	-0.6	-5.2
122	GGACTTTCAAGGCCCTGGGA	-10.4	-28.4	77.8	-17.5	0	-8.3

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intra-molecular oligo	kcal/mol Inter-molecular oligo
	SEQ.ID.NO:604 GCGGGGCTTCTTTGTTACAG						
673	SEQ.ID.NO:605 TCACATTTTTTCTCAGTCGC	-10.4	-26.4	75.7	-16	0	-3.4
971	SEQ.ID.NO:606 TGTTATATGAATCCATAATA	-10.4	-23.1	69.7	-12.7	0	-2.7
1118	SEQ.ID.NO:607 CATACTCCTCTTGAGTCATT	-10.4	-16.4	52.6	-5.3	-0.5	-3.6
1481	SEQ.ID.NO:608 CTCTCTATCCTTTATGTATT	-10.4	-23.2	69.7	-11.1	-1.7	-5.8
1540	SEQ.ID.NO:609 CAGTTGTGGAAGTTACACAT	-10.4	-21.4	66.1	-11	0	-1.2
1901	SEQ.ID.NO:610 ATATTTACAGTTGTGGAAGT	-10.4	-21.1	64	-9	-1.7	-5.9
1908	SEQ.ID.NO:611 GATTCCCTGGAGCCTTTTAA	-10.4	-19.3	60.6	-8.9	0	-3.4
1963	SEQ.ID.NO:612 TAAGATGAGCAAAATGAGAT	-10.4	-25.8	72.3	-15.4	0	-4.5
2060	SEQ.ID.NO:613 CCAGAGGCTCTGTCTCCACA	-10.4	-15.8	50.8	-5.4	0	-4.1
741	SEQ.ID.NO:614 ACATTTTTTCTCAGTCGCTT	-10.3	-29	82.1	-17.1	-1.5	-8
969	SEQ.ID.NO:615 CATTCACGGTCTGATCTGCA	-10.3	-23	69.3	-12.7	0	-3.1
998	SEQ.ID.NO:616 ACTTGTCGCAAGTCACGACC	-10.3	-25	72	-14.7	0	-4.9
1029	SEQ.ID.NO:617 GACCCTTTCAGCAAAGCAAT	-10.3	-25.5	71	-12.4	-2.8	-10.6
1302	SEQ.ID.NO:618 CTTCCAATAGGTCAGAATGC	-10.3	-23.9	66.9	-12.7	-0.8	-4.7
1382	SEQ.ID.NO:619 TCCTTTATGTATTGTCTATC	-10.3	-22.3	65.8	-11.4	-0.3	-3.6
1533	SEQ.ID.NO:620 CAGATTAATATGAGAGAGAA	-10.3	-20.8	65.3	-10.5	0	-0.9
1805	SEQ.ID.NO:621 GAAGTTACACATGTAATTAC	-10.3	-15.8	51.6	-5.5	0	-5.4
1893	SEQ.ID.NO:622 TGTTCTATCTAGCCCAATAT	-10.3	-16.9	54.3	-6	-0.3	-7.3
1924	SEQ.ID.NO:623 GATTTTCCCTAGTTCAACAG	-10.3	-22.8	67.2	-12.5	0	-3.7
2043	SEQ.ID.NO:624 CTCCTTGGATTGTTTTGGGT	-10.3	-22.5	66.7	-12.2	0	-3.6
149	SEQ.ID.NO:625 TCCAGGAAACTAAGAGAAGC	-10.2	-25.3	74.1	-15.1	0	-4.6
237	SEQ.ID.NO:626 AATGTTCAATGAGATTCATT	-10.2	-19.9	59.4	-9.1	-0.3	-4.7
365	SEQ.ID.NO:627 TCAGGCTGCTGGGGGTAGAA	-10.2	-17.5	55.6	-5.7	-1.5	-5.9
567	SEQ.ID.NO:628 TCTCCTGAAGAAACCTTTAC	-10.2	-27.3	78.1	-15.6	-1.4	-6.1
793	SEQ.ID.NO:629 GTCTTCATTCACGGTCTGAT	-10.2	-20.9	61.7	-10.7	0	-2.8
1003	SEQ.ID.NO:630 TATGAATCCATAATAAAATG	-10.2	-24.2	72.1	-14	0	-3.5
1113	SEQ.ID.NO:631	-10.2	-13.3	45.6	-2.4	-0.5	-3.3

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intra-molecular oligo	kcal/mol Inter-molecular oligo
1349	TCTTATTGAAAATCTCAGCT SEQ.ID.NO:632	-10.2	-18.8	58.5	-8.1	-0.1	-4.3
1474	CTCTTGAGTCATTTTCAGTT SEQ.ID.NO:633	-10.2	-21.9	68.6	-11.7	0	-5.8
1475	CCTCTTGAGTCATTTTCAGT SEQ.ID.NO:634	-10.2	-23.8	72.3	-13.1	-0.2	-5.5
1951	CCTTTTAAAACACAATGTAG SEQ.ID.NO:635	-10.2	-16.8	52.7	-6.1	-0.2	-6.2
1972	AGAATGCAGGATTCCCTGGA SEQ.ID.NO:636	-10.2	-25.4	71.3	-12.2	-3	-8.5
600	CTGAGTTCATATATTCCAGG SEQ.ID.NO:637	-10.1	-21.7	65.7	-11.6	0	-3.6
1259	GAAATCCTGGTAGCTTTTTT SEQ.ID.NO:638	-10.1	-21.8	65	-11.7	0	-4.7
1262	TCTGAAATCCTGGTAGCTTT SEQ.ID.NO:639	-10.1	-22.8	67.3	-12.7	0	-4.7
1278	TCTTCATGGTCCAAAGTCTG SEQ.ID.NO:640	-10.1	-23.1	68.8	-13	0	-4.7
1617	TGAGGATTTTCAGGCTGGTG SEQ.ID.NO:641	-10.1	-24.1	71.6	-14	0	-3.8
1661	ATGTCCGTAATTCAGTCAGG SEQ.ID.NO:642	-10.1	-23.3	68.8	-13.2	0	-3.3
1773	CCCCTCCCCTGTAATCCCCA SEQ.ID.NO:643	-10.1	-35.5	86.8	-25.4	0	-1.5
1932	GAGAAAGTTGTTCTATCTAG SEQ.ID.NO:644	-10.1	-18.4	59	-6.8	-1.4	-5.9
1933	AGAGAAAGTTGTTCTATCTA SEQ.ID.NO:645	-10.1	-18.4	59	-6.8	-1.4	-5.5
1989	AACAGGGCTTGCCAATTAGA SEQ.ID.NO:646	-10.1	-23.6	67.2	-12.2	-1.2	-7.7
2009	ACAATCAATTTAATTAGGCA SEQ.ID.NO:647	-10.1	-17.3	54.3	-7.2	0	-4.1
2129	CTGTTGCCATTATGTTTGCT SEQ.ID.NO:648	-10.1	-24.6	71.8	-14.5	0	-3.6
52	TGCTCAGAATCCAATTTCGC SEQ.ID.NO:649	-10	-23.3	66.6	-12.6	-0.4	-4
124	ATGGACTTTCAAGGCCCTGG SEQ.ID.NO:650	-10	-26.6	73.8	-16.6	0	-7.1
205	GAGCTATGTTTCTAAGTCTT SEQ.ID.NO:651	-10	-21.3	66.6	-11.3	0	-5.1
359	CAATGAGATTCATTTTTGAT SEQ.ID.NO:652	-10	-17.4	55.2	-5.7	-1.7	-6.2
447	CCCAGAGGACCTGCCACTTG SEQ.ID.NO:653	-10	-29.9	79.2	-18.8	-1	-4.9
579	GAGTACCACTCTTCAGGCTG SEQ.ID.NO:654	-10	-25.9	75.9	-14.4	-1.4	-6.5
711	AGCTCATCCCCTTTGATCCT SEQ.ID.NO:655	-10	-29.2	80.5	-19.2	0	-4.3
794	TTCTCCTGAAGAAACCTTTA SEQ.ID.NO:656	-10	-20.8	61.5	-9.9	-0.8	-3.6
973	CTTCACATTTTTTCTCAGTC SEQ.ID.NO:657	-10	-21.5	67.5	-11.5	0	-2.5
1260	TGAAATCCTGGTAGCTTTTT SEQ.ID.NO:658	-10	-21.7	64.6	-11.7	0	-4.7
1285	AATCTGGTCTTCATGGTCCA	-10	-25	73.6	-15	0	-4.7

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intra-molecular oligo	kcal/mol Inter-molecular oligo
	SEQ.ID.NO:659						
1363	CCCAGACGGAAGTTTCTTAT SEQ.ID.NO:660	-10	-23.9	67.7	-13.4	-0.2	-5.1
1563	GGCTCCTGAAGCTTCTCTAC SEQ.ID.NO:661	-10	-26.4	76.8	-14.3	-2.1	-10.8
1681	CTCAGCGTGGTGATGATTGA SEQ.ID.NO:662	-10	-24.1	69.9	-13.1	-0.9	-4.8
1685	GCATCTCAGCGTGGTGATGA SEQ.ID.NO:663	-10	-26.3	75.5	-14.9	-1.3	-6.7
1788	GAAAAAGGAGCTAGACCCCT SEQ.ID.NO:664	-10	-23.7	65.5	-13.7	0	-5.8
68	GCGATTTTGCTACAAATGCT SEQ.ID.NO:665	-9.9	-22.1	63.5	-10.8	-1.3	-6.5
129	CAGAGATGGACTTTCAAGGC SEQ.ID.NO:666	-9.9	-22.4	66.5	-12	-0.1	-4.1
206	TGAGCTATGTTTCTAAGTCT SEQ.ID.NO:667	-9.9	-21.2	66.1	-11.3	0	-5.1
487	ATTGCTGTATTGCGAGTATG SEQ.ID.NO:668	-9.9	-21.9	65.3	-11.1	-0.7	-4.1
1218	ACATGATTGGTTGCCATTTC SEQ.ID.NO:669	-9.9	-23.2	68.2	-12.6	-0.4	-5.9
1263	GTCTGAAATCCTGGTAGCTT SEQ.ID.NO:670	-9.9	-23.9	70.3	-14	0	-4.7
1274	CATGGTCCAAAGTCTGAAAT SEQ.ID.NO:671	-9.9	-20.5	60.6	-10.6	0	-3.9
1310	CAACCGCAGACCCCTTTCAGC SEQ.ID.NO:672	-9.9	-28.3	75.2	-18.4	0	-3.6
1389	ATTCTTTCTTCCAATAGGTC SEQ.ID.NO:673	-9.9	-21.9	67.3	-11.4	-0.3	-3.6
1619	GTTGAGGATTTTCAGGCTGG SEQ.ID.NO:674	-9.9	-24.2	72.2	-14.3	0	-5.8
1621	GTGTTGAGGATTTTCAGGCT SEQ.ID.NO:675	-9.9	-24.2	73	-14.3	0	-5.8
1898	TTGTGGAAGTTACACATGTA SEQ.ID.NO:676	-9.9	-20.1	61.8	-8.5	-1.7	-6.5
111	GCCCTGGGAGGATTCTGGAC SEQ.ID.NO:677	-9.8	-28.9	80	-18.3	-0.6	-8.3
200	ATGTTTCTAAGTCTTCTTTT SEQ.ID.NO:678	-9.8	-19.9	63.7	-9.5	-0.3	-2.7
599	TGAGTTCATATATTCCAGGA SEQ.ID.NO:679	-9.8	-21.4	65.1	-11.6	0	-4.9
813	ACAGCGTTTTTGGTAATGCT SEQ.ID.NO:680	-9.8	-23.2	67.7	-12	-1.3	-5.3
874	TTGACACTTTCTTCGCATGT SEQ.ID.NO:681	-9.8	-23.2	68.3	-13.4	0	-4.8
1004	TGTCTTCATTCACGGTCTGA SEQ.ID.NO:682	-9.8	-24.2	71.9	-14.4	0	-3.5
1031	TCACTTGTCGCAAGTCACGA SEQ.ID.NO:683	-9.8	-24.4	69.5	-12.4	-2.2	-10.8
1114	ATATGAATCCATAATAAAAT SEQ.ID.NO:684	-9.8	-13.3	45.6	-2.4	-1	-3.8
1271	GGTCCAAAGTCTGAAATCCT SEQ.ID.NO:685	-9.8	-23.1	66.4	-13.3	0	-3
1348	CTTATTGAAAATCTCAGCTG SEQ.ID.NO:686	-9.8	-18.4	57.1	-8.1	0	-8

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intra-molecular oligo	kcal/mol Inter-molecular oligo
1537	TCTATCCTTTATGTATTGTC SEQ.ID.NO:687	-9.8	-20.8	65.3	-11	0	-1.2
1545	ACTGCCTCTCTATCCTTTAT SEQ.ID.NO:688	-9.8	-25.3	73.9	-15.5	0	-3
1601	GGTGAATCTTACACAACTTT SEQ.ID.NO:689	-9.8	-19.8	60.3	-8.4	-1.6	-4.8
1807	ATCAGATTAATATGAGAGAG SEQ.ID.NO:690	-9.8	-16.3	53.3	-6.5	0	-7
1897	TGTGGAAGTTACACATGTAA SEQ.ID.NO:691	-9.8	-19.3	59.4	-7.9	-1.5	-6.9
1930	GAAAGTTGTTCTATCTAGCC SEQ.ID.NO:692	-9.8	-21.6	65.8	-11.3	-0.1	-3.9
2059	AAGATGAGCAAAATGAGATT SEQ.ID.NO:693	-9.8	-16.2	51.6	-6.4	0	-4.1
63	TTTGCTACAAATGCTCAGAA SEQ.ID.NO:694	-9.7	-19.8	59.6	-9.4	-0.4	-5.2
102	GGATTCTGGACTGAGTCTTC SEQ.ID.NO:695	-9.7	-23.7	72.3	-13	-0.9	-5.9
143	GGATTGTTTTGGGTCAGAGA SEQ.ID.NO:696	-9.7	-23.3	70.5	-13.6	0	-3.4
163	ACGATGTCTTCTACCTCCTT SEQ.ID.NO:697	-9.7	-25.7	73.5	-16	0	-3.5
228	CTAAGAGAAGCAGTGTTCAC SEQ.ID.NO:698	-9.7	-20.7	63.5	-10.3	-0.4	-6.8
319	GAAATGCACTTTCTTTATGG SEQ.ID.NO:699	-9.7	-19.4	59.3	-8.7	-0.9	-8.4
734	CTCTGTCTCCACAAACAACA SEQ.ID.NO:700	-9.7	-22.4	64.8	-12.2	-0.1	-2.9
902	TCTCTTTGCATTTCCTTAGT SEQ.ID.NO:701	-9.7	-23.8	72.2	-14.1	0	-5.1
1125	CTCTGTTTGTTATATGAATC SEQ.ID.NO:702	-9.7	-18.6	59.3	-8.9	0	-2.4
1155	AAAATTTTATTTGTTATTTC SEQ.ID.NO:703	-9.7	-13.7	47.7	-3.5	-0.2	-6.3
1256	ATCCTGGTAGCTTTTTTGTG SEQ.ID.NO:704	-9.7	-23.8	71.5	-14.1	0	-4.7
1372	GTCAGAATGCCCAGACGGAA SEQ.ID.NO:705	-9.7	-25.4	69.4	-15	-0.4	-4.8
1432	AAACATAGGTGTTATATATT SEQ.ID.NO:706	-9.7	-16.1	52.6	-4.7	-1.7	-7.4
1602	TGGTGAATCTTACACAACTT SEQ.ID.NO:707	-9.7	-19.7	59.9	-8.4	-1.6	-4.8
1764	TGTAATCCCCATCACTGCAC SEQ.ID.NO:708	-9.7	-26.2	72.6	-16.5	0	-4.8
168	CTTCTACGATGTCTTCTACC SEQ.ID.NO:709	-9.6	-23.4	69.2	-13.8	0	-3.5
445	CAGAGGACCTGCCACTTGTT SEQ.ID.NO:710	-9.6	-27.2	76.2	-16.5	-1	-4.9
659	TTACAGGCATCTCTGCTACC SEQ.ID.NO:711	-9.6	-25.6	74.4	-13.8	-2.2	-5.6
1015	ACGACCTTCACTGTCTTCAT SEQ.ID.NO:712	-9.6	-24.7	71.3	-14.4	-0.5	-3.7
1030	CACTTGTCGCAAGTCACGAC SEQ.ID.NO:713	-9.6	-24.2	68.5	-12.4	-2.2	-10.8
1094	GTAGAAGAGTCTGTTGATCT	-9.6	-21.1	66.3	-11	-0.2	-5.3

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intra-molecular oligo	kcal/mol Inter-molecular oligo
	SEQ.ID.NO:714 GATTGGTTGCCATTTCCGTC						
1214	SEQ.ID.NO:715 TCCAATAGGTCAGAATGCCC	-9.6	-26.7	75.3	-16.4	-0.4	-4.6
1380	SEQ.ID.NO:716 ACAGGGCTTGCCAATTAGAA	-9.6	-25.3	70.7	-14.2	-1.4	-5
1988	SEQ.ID.NO:717 AGATGAGCAAAATGAGATTT	-9.6	-23.6	67.2	-12.2	-1.8	-8.5
2058	SEQ.ID.NO:718 TTTGCTTTATTGCCAAGATT	-9.6	-17	53.6	-7.4	0	-4.1
2115	SEQ.ID.NO:719 AGAGATGGACTTTCAAGGCC	-9.6	-21.4	63.6	-11.8	0	-3.6
128	SEQ.ID.NO:720 GAGGACCTGCCACTTGTTCT	-9.5	-23.7	69.1	-14.2	0	-6.4
443	SEQ.ID.NO:721 ACATTGCTGTATTGCGAGTA	-9.5	-27.8	78.5	-17.2	-1	-4
489	SEQ.ID.NO:722 AAATCCTGGTAGCTTTTTTG	-9.5	-22.8	67.2	-13.3	0	-4.1
1258	SEQ.ID.NO:723 GTCTTCATGGTCCAAAGTCT	-9.5	-21.2	63.6	-11.7	0	-4.7
1279	SEQ.ID.NO:724 ATCTGGTCTTCATGGTCCAA	-9.5	-24.3	72.4	-14.8	0	-4.2
1284	SEQ.ID.NO:725 TACTGCCTCTCTATCCTTTA	-9.5	-25	73.6	-15	-0.2	-4.7
1546	SEQ.ID.NO:726 GTCCGTAATTCAGTCAGGCG	-9.5	-25	73.4	-15.5	0	-3
1659	SEQ.ID.NO:727 ACAGTTGTGGAAGTTACACA	-9.5	-25.9	73.3	-16.4	0	-4
1902	SEQ.ID.NO:728 TATTTACAGTTGTGGAAGTT	-9.5	-21.3	64.6	-10.5	-1.2	-6.1
1907	SEQ.ID.NO:729 GTTCTATCTAGCCCAATATT	-9.5	-19.4	61	-9.9	0	-3.1
1923	SEQ.ID.NO:730 TGTAGAGAAAGTTGTTCTAT	-9.5	-22.9	67.7	-13.4	0	-3.8
1936	SEQ.ID.NO:731 CTTTTTTGTGAATTCTACAA	-9.5	-18.3	58.6	-7.9	-0.8	-4.4
1246	SEQ.ID.NO:732 TTCTTATTGAAAATCTCAGC	-9.4	-17.8	56.4	-7.4	-0.2	-9.8
1350	SEQ.ID.NO:733 CTTACACAACTTTTGTAGCA	-9.4	-18	56.8	-8.1	-0.1	-3.1
1594	SEQ.ID.NO:734 GAATCTTACACAACTTTTGT	-9.4	-20.6	62.4	-10.3	-0.7	-5.8
1598	SEQ.ID.NO:735 GTGAATCTTACACAACTTTT	-9.4	-18.7	58.1	-8.4	-0.7	-3.9
1600	SEQ.ID.NO:736 AGCCCAATATTTACAGTTGT	-9.4	-18.7	58.1	-8.4	-0.8	-4.3
1914	SEQ.ID.NO:737 CAGGGCTTGCCAATTAGAAT	-9.4	-22.8	66.8	-13.4	0	-3.9
1987	SEQ.ID.NO:738 ACCTCCTTGGATTGTTTTGG	-9.4	-23.4	66.6	-12.2	-1.8	-8.5
151	SEQ.ID.NO:739 TCTACGATGTCTTCTACCTC	-9.3	-25.1	72.3	-15.1	-0.5	-4.6
166	SEQ.ID.NO:740 GTCTGAAGTTTCATCTTGAG	-9.3	-23.7	70.4	-14.4	0	-3.5
274	SEQ.ID.NO:741	-9.3	-20.9	65.4	-11.6	0	-4.7

position	oligo	kcal/ mol total binding	kcal/ mol duplex forma- tion	deg C Tm of Duplex	kcal/ mol target struc- ture	kcal/ mol Intra- mole- cular oligo	kcal/ mol Inter- mole- cular oligo
275	TGTCTGAAGTTTCATCTTGA SEQ.ID.NO:742	-9.3	-20.9	65	-11.6	0	-4.7
580	AGAGTACCACTCTTCAGGCT SEQ.ID.NO:743	-9.3	-25.9	76.4	-14.4	-2.2	-8
657	ACAGGCATCTCTGCTACCTC SEQ.ID.NO:744	-9.3	-27.1	78.5	-15.6	-2.2	-5.6
658	TACAGGCATCTCTGCTACCT SEQ.ID.NO:745	-9.3	-26.4	76.1	-15.6	-1.4	-5.6
834	CCCCCGTTTTACACTTGTA SEQ.ID.NO:746	-9.3	-27.1	73.6	-17.8	0.1	-4.3
1209	GTTGCCATTTCCGTCAAAAT SEQ.ID.NO:747	-9.3	-23.4	65.7	-14.1	0	-3
1217	CATGATTGGTTGCCATTTCC SEQ.ID.NO:748	-9.3	-25	71.3	-15	-0.4	-4.6
1268	CCAAAGTCTGAAATCCTGGT SEQ.ID.NO:749	-9.3	-22.7	64.8	-13.4	0	-4.6
1269	TCCAAAGTCTGAAATCCTGG SEQ.ID.NO:750	-9.3	-21.9	63.2	-12.6	0	-4
1362	CCAGACGGAAGTTTCTTATT SEQ.ID.NO:751	-9.3	-22	64.5	-11.8	-0.8	-5.1
1393	TCGAATTCTTTCTTCCAATA SEQ.ID.NO:752	-9.3	-20.2	60.7	-10.1	-0.6	-6.4
1433	TAAACATAGGTGTTATATAT SEQ.ID.NO:753	-9.3	-15.7	51.7	-4.7	-1.7	-7.2
1772	CCCTCCCCTGTAATCCCCAT SEQ.ID.NO:754	-9.3	-33.5	83.7	-24.2	0	-1.6
1851	TCTTGAGTGAAACTGGGTAC SEQ.ID.NO:755	-9.3	-21	63.7	-11	-0.5	-5.2
1863	TTCATCAAGATTTCTTGAGT SEQ.ID.NO:756	-9.3	-19.6	61.7	-7.9	-2.4	-11.2
1973	TAGAATGCAGGATTCCCTGG SEQ.ID.NO:757	-9.3	-24.5	69.5	-12.2	-3	-8.5
2019	AATTGAAGTAACAATCAATT SEQ.ID.NO:758	-9.3	-14.2	47.7	-2.7	-2.2	-7.1
2108	TATTGCCAAGATTGAATACA SEQ.ID.NO:759	-9.3	-18.8	57	-9.5	0	-3.7
616	CTCAGCTGGCATACGCCTGA SEQ.ID.NO:760	-9.2	-28.4	77.6	-16.3	-2.9	-9.9
740	CAGAGGCTCTGTCTCCACAA SEQ.ID.NO:761	-9.2	-26.3	75.7	-15.9	-1.1	-7.2
1149	TTATTTGTTATTTCCTGAGG SEQ.ID.NO:762	-9.2	-20.3	62.8	-11.1	0	-3.5
1637	CCAGGAGACAGGCAAAGTGT SEQ.ID.NO:763	-9.2	-24.7	70.4	-15.5	0	-4
1840	ACTGGGTACAAGTGAAATAA SEQ.ID.NO:764	-9.2	-18	55.6	-8.8	0	-5
2008	CAATCAATTTAATTAGGCAA SEQ.ID.NO:765	-9.2	-16.4	52.1	-7.2	0	-4.1
669	GGCTTCTTTGTTACAGGCAT SEQ.ID.NO:766	-9.1	-25.1	74.3	-15.3	-0.4	-4.2
1032	GTCACTTGTCGCAAGTCACG SEQ.ID.NO:767	-9.1	-25	71.5	-13.7	-2.2	-10.8
1265	AAGTCTGAAATCCTGGTAGC SEQ.ID.NO:768	-9.1	-22.2	65.9	-13.1	0	-4.6
1347	TTATTGAAAATCTCAGCTGA	-9.1	-18.1	56.5	-8.1	-0.1	-9.8

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intramolecular oligo	kcal/mol Intermolecular oligo
	SEQ.ID.NO:769						
1596	ATCTTACACAACTTTTGTAG SEQ.ID.NO:770	-9.1	-18.5	58.4	-8.4	-0.9	-4.3
1599	TGAATCTTACACAACTTTTG SEQ.ID.NO:771	-9.1	-17.5	55.1	-8.4	0	-2.9
1850	CTTGAGTGAAACTGGGTACA SEQ.ID.NO:772	-9.1	-21.3	63.4	-11	-1.1	-6.3
1853	TTTCTTGAGTGAAACTGGGT SEQ.ID.NO:773	-9.1	-21.3	64.4	-11	-1.1	-5.1
1962	ATTCCCTGGAGCCTTTTAAA SEQ.ID.NO:774	-9.1	-24.5	68.8	-15.4	0	-4.5
2104	GCCAAGATTGAATACAACTC SEQ.ID.NO:775	-9.1	-19.8	59	-9.8	-0.8	-3.7
84	TCCTCTCCAGATCCCAGCGA SEQ.ID.NO:776	-9	-30.6	82	-21.6	0	-4.5
132	GGTCAGAGATGGACTTTCAA SEQ.ID.NO:777	-9	-22.2	66.8	-12	-1.1	-5
201	TATGTTTCTAAGTCTTCTTT SEQ.ID.NO:778	-9	-19.5	62.7	-9.9	-0.3	-2.7
488	CATTGCTGTATTGCGAGTAT SEQ.ID.NO:779	-9	-22.6	66.6	-12.7	-0.7	-4.1
493	CTGAACATTGCTGTATTGCG SEQ.ID.NO:780	-9	-22.1	64	-12.2	-0.7	-4.5
1156	TAAAATTTTATTTGTTATTT SEQ.ID.NO:781	-9	-13	46.1	-3.5	-0.2	-7.5
1541	CCTCTCTATCCTTTATGTAT SEQ.ID.NO:782	-9	-23.3	69.7	-14.3	0	-1.2
1622	AGTGTTGAGGATTTTCAGGC SEQ.ID.NO:783	-9	-23.3	71.2	-14.3	0	-5.6
1715	ACTTGTGGTCGTTTACTCTC SEQ.ID.NO:784	-9	-23.9	72.5	-14.9	0	-3.3
1803	GATTAATATGAGAGAGAAAA SEQ.ID.NO:785	-9	-13.7	46.9	-4.7	0	-4.7
110	CCCTGGGAGGATTCTGGACT SEQ.ID.NO:786	-8.9	-28	77.6	-18.3	-0.6	-7.2
853	CATATCCATCACACAGTTGC SEQ.ID.NO:787	-8.9	-23.5	68.8	-14.6	0	-2.6
1016	CACGACCTTCACTGTCTTCA SEQ.ID.NO:788	-8.9	-25.4	72.4	-15.8	-0.5	-3.7
1038	GTCGAGGTCACTTGTCGCAA SEQ.ID.NO:789	-8.9	-25.9	73.7	-16.3	-0.4	-5.4
1157	TTAAAATTTTATTTGTTATT SEQ.ID.NO:790	-8.9	-13	46.1	-3.5	-0.2	-8
1158	TTTAAAATTTTATTTGTTAT SEQ.ID.NO:791	-8.9	-13	46.1	-3.5	-0.2	-8
1270	GTCCAAAGTCTGAAATCCTG SEQ.ID.NO:792	-8.9	-21.9	63.8	-13	0	-3
1308	ACCGCAGACCCTTTCAGCAA SEQ.ID.NO:793	-8.9	-28.3	75.2	-18.3	-1	-4.1
1476	TCCTCTTGAGTCATTTTCAG SEQ.ID.NO:794	-8.9	-23	70.4	-13.6	-0.2	-5.8
1539	TCTCTATCCTTTATGTATTG SEQ.ID.NO:795	-8.9	-20.5	63.9	-11.6	0	-1.2
1757	CCCATCACTGCACGTCCCAG SEQ.ID.NO:796	-8.9	-30.7	80.1	-21.3	-0.1	-7

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intra-molecular oligo	kcal/mol Inter-molecular oligo
1804	AGATTAATATGAGAGAGAAA SEQ.ID.NO:797	-8.9	-14.4	48.6	-5.5	0	-4.7
1976	AATTAGAATGCAGGATTCCC SEQ.ID.NO:798	-8.9	-21.8	63.4	-12.2	-0.5	-5.8
94	GACTGAGTCTTCCTCTCCAG SEQ.ID.NO:799	-8.8	-26.6	78.3	-16.5	-1.2	-5.3
366	GAATGTTCAATGAGATTCAT SEQ.ID.NO:800	-8.8	-18	56.6	-8.3	-0.8	-7
619	AGTCTCAGCTGGCATACGCC SEQ.ID.NO:801	-8.8	-28.5	80.1	-17.6	-2.1	-9.3
652	CATCTCTGCTACCTCAGTTT SEQ.ID.NO:802	-8.8	-25.3	75	-16.5	0.4	-3.6
1283	TCTGGTCTTCATGGTCCAAA SEQ.ID.NO:803	-8.8	-24.3	71.1	-15	-0.2	-4.7
1309	AACCGCAGACCCTTTCAGCA SEQ.ID.NO:804	-8.8	-28.3	75.2	-18.4	-1	-4.1
1383	TCTTCCAATAGGTCAGAATG SEQ.ID.NO:805	-8.8	-20.9	63.1	-11.4	-0.4	-3.7
1549	CTCTACTGCCTCTCTATCCT SEQ.ID.NO:806	-8.8	-27.3	79.1	-18.5	0	-3
1956	TGGAGCCTTTTAAAACACAA SEQ.ID.NO:807	-8.8	-19.5	57.7	-10.7	0	-6.2
1959	CCCTGGAGCCTTTTAAAACA SEQ.ID.NO:808	-8.8	-24.2	66.6	-15.4	0	-6.2
2049	AAATGAGATTTTCCCTAGTT SEQ.ID.NO:809	-8.8	-20.4	61.3	-11.6	0	-3.8
150	CCTCCTTGGATTGTTTTGGG SEQ.ID.NO:810	-8.7	-26.1	74.3	-17.4	0	-4.6
171	CTCCTTCTACGATGTCTTCT SEQ.ID.NO:811	-8.7	-24.8	72.8	-16.1	0	-3.5
436	TGCCACTTGTTCTGTTAAAA SEQ.ID.NO:812	-8.7	-21.2	62.8	-12.5	0	-3
645	GCTACCTCAGTTTCTCCCTG SEQ.ID.NO:813	-8.7	-28.6	81.3	-19.9	0	-3.2
646	TGCTACCTCAGTTTCTCCCT SEQ.ID.NO:814	-8.7	-28.6	81.3	-19.9	0	-3.6
647	CTGCTACCTCAGTTTCTCCC SEQ.ID.NO:815	-8.7	-28.6	81.3	-19.9	0	-3.6
743	ATCCAGAGGCTCTGTCTCCA SEQ.ID.NO:816	-8.7	-28.5	82.2	-18.2	-1.5	-8
795	CTTCTCCTGAAGAAACCTTT SEQ.ID.NO:817	-8.7	-22	63.9	-11.7	-1.5	-5.3
803	TGGTAATGCTTCTCCTGAAG SEQ.ID.NO:818	-8.7	-22.7	66.8	-12.2	-1.8	-6.1
996	TTCACGGTCTGATCTGCATG SEQ.ID.NO:819	-8.7	-24.3	70.7	-15.6	0	-4.9
1106	CCATAATAAAATGTAGAAGA SEQ.ID.NO:820	-8.7	-14.7	48.4	-6	0	-2.8
1230	ACAAGAACCTGTACATGATT SEQ.ID.NO:821	-8.7	-19.7	59.1	-11	0	-6.1
1272	TGGTCCAAAGTCTGAAATCC SEQ.ID.NO:822	-8.7	-22.2	64.4	-13.5	0	-3.5
1280	GGTCTTCATGGTCCAAAGTC SEQ.ID.NO:823	-8.7	-24.6	73.1	-15.9	0	-4.7
1538	CTCTATCCTTTATGTATTGT	-8.7	-21.3	65.7	-12.6	0	-1.2

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intramolecular oligo	kcal/mol Intermolecular oligo
	SEQ.ID.NO:824						
1562	GCTCCTGAAGCTTCTCTACT SEQ.ID.NO:825	-8.7	-26.1	76.2	-15.8	-1.3	-10.8
1620	TGTTGAGGATTTTCAGGCTG SEQ.ID.NO:826	-8.7	-23	69.3	-14.3	0	-5.8
1676	CGTGGTGATGATTGAATGTC SEQ.ID.NO:827	-8.7	-21.2	63.2	-12.5	0	-2.8
1758	CCCCATCACTGCACGTCCCA SEQ.ID.NO:828	-8.7	-32.7	83	-24	0	-4.8
1762	TAATCCCCATCACTGCACGT SEQ.ID.NO:829	-8.7	-27	72.7	-18.3	0	-4.8
1852	TTCTTGAGTGAAACTGGGTA SEQ.ID.NO:830	-8.7	-20.9	63.5	-11	-1.1	-4.4
1957	CTGGAGCCTTTTAAAACACA SEQ.ID.NO:831	-8.7	-21.1	61.3	-12.4	0	-6.2
2010	AACAATCAATTTAATTAGGC SEQ.ID.NO:832	-8.7	-15.9	51.3	-7.2	0	-4.1
83	CCTCTCCAGATCCCAGCGAT SEQ.ID.NO:833	-8.6	-30.2	80.2	-21.6	0	-4.5
86	CTTCCTCTCCAGATCCCAGC SEQ.ID.NO:834	-8.6	-30.2	83.6	-21.6	0	-4.5
103	AGGATTCTGGACTGAGTCTT SEQ.ID.NO:835	-8.6	-23.3	70.8	-13.7	-0.9	-5.9
139	TGTTTTGGGTCAGAGATGGA SEQ.ID.NO:836	-8.6	-23.2	70	-13.7	-0.7	-3.6
444	AGAGGACCTGCCACTTGTTC SEQ.ID.NO:837	-8.6	-26.9	76.8	-17.2	-1	-3.9
569	CTTCAGGCTGCTGGGGGTAG SEQ.ID.NO:838	-8.6	-28.4	81.9	-18.3	-1.4	-6.1
742	TCCAGAGGCTCTGTCTCCAC SEQ.ID.NO:839	-8.6	-28.7	83	-18.5	-1.5	-8
921	CATTCAGCCAACATTCCCAT SEQ.ID.NO:840	-8.6	-25.8	71	-17.2	0	-3.2
1273	ATGGTCCAAAGTCTGAAATC SEQ.ID.NO:841	-8.6	-20.2	60.7	-11.6	0	-3.9
1290	AAAGCAATCTGGTCTTCATG SEQ.ID.NO:842	-8.6	-20.6	62.2	-12	0	-4.1
1296	TTCAGCAAAGCAATCTGGTC SEQ.ID.NO:843	-8.6	-22.2	66	-12.7	-0.7	-4.4
1424	GTGTTATATATTCATCAGAG SEQ.ID.NO:844	-8.6	-18.5	59.6	-9.9	0	-4
1544	CTGCCTCTCTATCCTTTATG SEQ.ID.NO:845	-8.6	-25.1	73.1	-16.5	0	-3
1618	TTGAGGATTTTCAGGCTGGT SEQ.ID.NO:846	-8.6	-24.2	72.2	-15.6	0	-5.8
1677	GCGTGGTGATGATTGAATGT SEQ.ID.NO:847	-8.6	-22.6	65.8	-14	0	-3.5
1844	TGAAACTGGGTACAAGTGAA SEQ.ID.NO:848	-8.6	-18.9	57.3	-10.3	0	-6
1858	CAAGATTTCTTGAGTGAAAC SEQ.ID.NO:849	-8.6	-17.4	55.1	-7.9	-0.8	-8.1
1974	TTAGAATGCAGGATTCCCTG SEQ.ID.NO:850	-8.6	-23.4	67.3	-12.2	-2.6	-7.2
2100	AGATTGAATACAACTCTTTA SEQ.ID.NO:851	-8.6	-16.8	54	-7.1	-1	-3.6

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intra-molecular oligo	kcal/mol Inter-molecular oligo
62	TTGCTACAAATGCTCAGAAT SEQ.ID.NO:852	-8.5	-19.7	59.2	-10.5	-0.4	-3.6
85	TTCCTCTCCAGATCCCAGCG SEQ.ID.NO:853	-8.5	-30.1	81.1	-21.6	0	-4.5
148	TCCTTGGATTGTTTTGGGTC SEQ.ID.NO:854	-8.5	-24.8	73.8	-16.3	0	-4.3
165	CTACGATGTCTTCTACCTCC SEQ.ID.NO:855	-8.5	-25.3	72.5	-16.8	0	-3.5
175	TTCACTCCTTCTACGATGTC SEQ.ID.NO:856	-8.5	-23.9	70.6	-15.4	0	-3.5
176	TTTCACTCCTTCTACGATGT SEQ.ID.NO:857	-8.5	-23.6	69.3	-15.1	0	-3.5
351	TTCATTTTTGATCCCATCCA SEQ.ID.NO:858	-8.5	-24.4	69.8	-15	-0.8	-4.3
484	GCTGTATTGCGAGTATGGTT SEQ.ID.NO:859	-8.5	-24.3	71.5	-15.8	0	-4.1
581	GAGAGTACCACTCTTCAGGC SEQ.ID.NO:860	-8.5	-25.6	75.7	-14.4	-2.7	-8.6
1009	TTCACTGTCTTCATTCACGG SEQ.ID.NO:861	-8.5	-23.4	69.4	-14.9	0	-3.5
1564	TGGCTCCTGAAGCTTCTCTA SEQ.ID.NO:862	-8.5	-26.2	76	-15.6	-2.1	-10.8
1615	AGGATTTTCAGGCTGGTGAA SEQ.ID.NO:863	-8.5	-23.4	69.3	-14.3	-0.3	-5.4
1753	TCACTGCACGTCCCAGATTT SEQ.ID.NO:864	-8.5	-26.8	74.4	-17.6	-0.5	-7.5
1890	GTTACACATGTAATTACAAC SEQ.ID.NO:865	-8.5	-17.2	54.6	-7.5	-0.3	-10.3
1960	TCCCTGGAGCCTTTTAAAAC SEQ.ID.NO:866	-8.5	-23.9	66.9	-15.4	0	-6.2
60	GCTACAAATGCTCAGAATCC SEQ.ID.NO:867	-8.4	-22	64	-13.6	0	-3.6
302	TGGTGGTCTTCAAAAAAAAC SEQ.ID.NO:868	-8.4	-16.6	52.3	-8.2	0	-2.9
643	TACCTCAGTTTCTCCCTGGT SEQ.ID.NO:869	-8.4	-28.3	81.1	-19.9	0.3	-4.8
1006	ACTGTCTTCATTCACGGTCT SEQ.ID.NO:870	-8.4	-24.7	73.4	-16.3	0	-3.5
1008	TCACTGTCTTCATTCACGGT SEQ.ID.NO:871	-8.4	-24.5	72.5	-16.1	0	-3.5
1080	TGATCTGGGGTGAGTTCAGT SEQ.ID.NO:872	-8.4	-24.9	75.3	-16	-0.2	-4.9
1314	GCTTCAACCGCAGACCCTTT SEQ.ID.NO:873	-8.4	-28.6	76.1	-20.2	0	-3.6
1547	CTACTGCCTCTCTATCCTTT SEQ.ID.NO:874	-8.4	-26.2	76	-17.8	0	-2.3
1597	AATCTTACACAACTTTTGTA SEQ.ID.NO:875	-8.4	-17.8	56.2	-8.4	-0.9	-4.3
1692	GACATCAGCATCTCAGCGTG SEQ.ID.NO:876	-8.4	-25.3	73.2	-15.9	-0.9	-4.1
1713	TTGTGGTCGTTTACTCTCCA SEQ.ID.NO:877	-8.4	-25.5	74.8	-16.6	-0.2	-3.7
1817	AAAGTTATACATCAGATTAA SEQ.ID.NO:878	-8.4	-15	50	-6.6	0	-3.4
1842	AAACTGGGTACAAGTGAAAT	-8.4	-17.6	54.4	-9.2	0	-6

position	oligo	kcal/ mol total binding	kcal/ mol duplex forma- tion	deg C Tm of Duplex	kcal/ mol target struc- ture	kcal/ mol Intra- mole- cular oligo	kcal/ mol Inter- mole- cular oligo
	SEQ.ID.NO:879						
	TTCCCTGGAGCCTTTTAAAA						
1961	SEQ.ID.NO:880	-8.4	-23.8	66.7	-15.4	0	-6
	AATGAGATTTTCCCTAGTTC						
2048	SEQ.ID.NO:881	-8.4	-21.5	64.9	-13.1	0	-3.8
	TGAGTCTTCCTCTCCAGATC						
91	SEQ.ID.NO:882	-8.3	-25.9	77.4	-16.3	-1.2	-5.9
	ACTTTCAAGGCCCTGGGAGG						
120	SEQ.ID.NO:883	-8.3	-27.8	76.8	-18.9	-0.2	-8.3
	TCACTCCTTCTACGATGTCT						
174	SEQ.ID.NO:884	-8.3	-24.7	72.2	-16.4	0	-3.5
	GTATTGCGAGTATGGTTCCA						
481	SEQ.ID.NO:885	-8.3	-24.7	71.8	-16.4	0	-5.3
	AACTGAACATTGCTGTATTG						
495	SEQ.ID.NO:886	-8.3	-19	58.2	-10	-0.5	-3.9
	GTTATATGAATCCATAATAA						
1117	SEQ.ID.NO:887	-8.3	-15.7	51	-6.3	-1	-4.2
	TCTCAGCTGAACGAAGGAAC						
1337	SEQ.ID.NO:888	-8.3	-21.2	62	-11.8	0	-10.1
	TTATGTATTGTCTATCTGGA						
1529	SEQ.ID.NO:889	-8.3	-20.1	63.3	-11.8	0	-2.7
	CTTCTCTACTGCCTCTCTAT						
1552	SEQ.ID.NO:890	-8.3	-25.4	75.7	-17.1	0	-3
	AACTTTTGTAGCACATCAAG						
1587	SEQ.ID.NO:891	-8.3	-19.4	59.7	-10.3	-0.6	-6.4
	CAGGCGACCCAGGAGACAGG						
1645	SEQ.ID.NO:892	-8.3	-28.5	76.4	-19.2	-0.9	-5.4
	AATGTCCGTAATTCAGTCAG						
1662	SEQ.ID.NO:893	-8.3	-21.4	63.9	-13.1	0	-3
	AGTGAAACTGGGTACAAGTG						
1846	SEQ.ID.NO:894	-8.3	-20.2	61.1	-11.1	-0.6	-6.6
	AAACAGGGCTTGCCAATTAG						
1990	SEQ.ID.NO:895	-8.3	-22.3	63.9	-12.2	-1.8	-8.5
	TGGTAAGATGAGCAAAATGA						
2063	SEQ.ID.NO:896	-8.3	-17.6	54.5	-9.3	0	-4.1
	CTGGACTGAGTCTTCCTCTC						
97	SEQ.ID.NO:897	-8.2	-26	77.7	-16.5	-1.2	-6.9
	CCTTCTACGATGTCTTCTAC						
169	SEQ.ID.NO:898	-8.2	-23.4	69.2	-15.2	0	-3.5
	ATGGTGGTCTTCAAAAAAAA						
303	SEQ.ID.NO:899	-8.2	-16.4	51.8	-8.2	0	-3.3
	GCATCTCTGCTACCTCAGTT						
653	SEQ.ID.NO:900	-8.2	-27	79.2	-17	-1.8	-5.6
	TCTTCGCATGTACATATCCA						
865	SEQ.ID.NO:901	-8.2	-23.7	68.7	-15	0	-8
	CTTCACTGTCTTCATTCACG						
1010	SEQ.ID.NO:902	-8.2	-23.1	68.8	-14.9	0	-3
	AATCCTGGTAGCTTTTTTGT						
1257	SEQ.ID.NO:903	-8.2	-23.1	69.2	-14.9	0	-4.7
	TGAAAATCTCAGCTGAACGA						
1343	SEQ.ID.NO:904	-8.2	-19.1	57	-9.8	0	-10.1
	ATCACTGCACGTCCCAGATT						
1754	SEQ.ID.NO:905	-8.2	-26.7	74	-17.8	-0.5	-7.5
	CAGGATTCCCTGGAGCCTTT						
1966	SEQ.ID.NO:906	-8.2	-28.6	78.8	-18.1	-2.3	-7.8

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intramolecular oligo	kcal/mol Intermolecular oligo
1975	ATTAGAATGCAGGATTCCCT SEQ.ID.NO:907	-8.2	-23.4	67.4	-13.8	-1.3	-6
130	TCAGAGATGGACTTTCAAGG SEQ.ID.NO:908	-8.1	-21	63.8	-12	-0.7	-4.8
131	GTCAGAGATGGACTTTCAAG SEQ.ID.NO:909	-8.1	-21	64.4	-12	-0.7	-4.4
566	CAGGCTGCTGGGGGTAGAAA SEQ.ID.NO:910	-8.1	-26.2	73.8	-17.2	-0.8	-6.1
615	TCAGCTGGCATACGCCTGAG SEQ.ID.NO:911	-8.1	-27.5	76	-16.5	-2.9	-9.9
617	TCTCAGCTGGCATACGCCTG SEQ.ID.NO:912	-8.1	-28.2	78	-17.2	-2.9	-9.8
707	CATCCCCTTTGATCCTCCCT SEQ.ID.NO:913	-8.1	-31.4	82.6	-23.3	0	-4.3
712	CAGCTCATCCCCTTTGATCC SEQ.ID.NO:914	-8.1	-29	79.6	-20.9	0	-4.4
751	ATAGTGGTATCCAGAGGCTC SEQ.ID.NO:915	-8.1	-25	74.9	-16.1	-0.6	-4.6
814	CACAGCGTTTTTGGTAATGC SEQ.ID.NO:916	-8.1	-23	66.9	-14.2	-0.5	-4.1
1013	GACCTTCACTGTCTTCATTC SEQ.ID.NO:917	-8.1	-24.2	72.8	-16.1	0	-3.6
1159	TTTTAAAATTTTATTTGTTA SEQ.ID.NO:918	-8.1	-13.1	46.3	-5	0.3	-8
1384	TTCTTCCAATAGGTCAGAAT SEQ.ID.NO:919	-8.1	-21	63.5	-11.4	-1.4	-4.7
1385	TTTCTTCCAATAGGTCAGAA SEQ.ID.NO:920	-8.1	-21.1	63.9	-11.4	-1.5	-4.8
1765	CTGTAATCCCCATCACTGCA SEQ.ID.NO:921	-8.1	-26.9	73.9	-18.8	0	-4.7
1777	TAGACCCCTCCCCTGTAATC SEQ.ID.NO:922	-8.1	-29.3	78.1	-21.2	0	-2
1845	GTGAAACTGGGTACAAGTGA SEQ.ID.NO:923	-8.1	-20.8	62.2	-12.7	0	-6
1892	AAGTTACACATGTAATTACA SEQ.ID.NO:924	-8.1	-17	54.3	-7.9	-0.3	-9.9
1997	ATTAGGCAAACAGGGCTTGC SEQ.ID.NO:925	-8.1	-24	68.9	-15	-0.8	-7.2
2012	GTAACAATCAATTTAATTAG SEQ.ID.NO:926	-8.1	-13.8	47.3	-5.7	0	-4.1
2099	GATTGAATACAACTCTTTAA SEQ.ID.NO:927	-8.1	-16.1	52.1	-7.1	-0.8	-3.7
2107	ATTGCCAAGATTGAATACAA SEQ.ID.NO:928	-8.1	-18.4	55.7	-9.5	-0.6	-4.2
236	CCAGGAAACTAAGAGAAGCA SEQ.ID.NO:929	-8	-20.2	59.3	-11.6	-0.3	-4.7
911	ACATTCCCATCTCTTTGCAT SEQ.ID.NO:930	-8	-25.4	72.9	-17.4	0	-5.1
933	TCAGTTAACAAGCATTCAGC SEQ.ID.NO:931	-8	-21.1	64	-12.4	-0.5	-8.3
961	TCTCAGTCGCTTAGATTTAC SEQ.ID.NO:932	-8	-22	67.3	-14	0	-3.1
1095	TGTAGAAGAGTCTGTTGATC SEQ.ID.NO:933	-8	-20.2	64	-11.7	-0.2	-5.8
1345	ATTGAAAATCTCAGCTGAAC	-8	-17.8	55.4	-8.1	-0.1	-11.6

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intra-molecular oligo	kcal/mol Inter-molecular oligo
	SEQ.ID.NO:934						
1766	CCTGTAATCCCCATCACTGC SEQ.ID.NO:935	-8	-28.2	76.3	-20.2	0	-2.6
1860	ATCAAGATTTCTTGAGTGAA SEQ.ID.NO:936	-8	-18.3	57.8	-7.9	-2.4	-11.2
1903	TACAGTTGTGGAAGTTACAC SEQ.ID.NO:937	-8	-20.3	62.8	-11.6	-0.4	-4.2
277	AGTGTCTGAAGTTTCATCTT SEQ.ID.NO:938	-7.9	-21.5	67.5	-13.6	0	-4.7
350	TCATTTTTGATCCCATCCAA SEQ.ID.NO:939	-7.9	-23.6	67.3	-15	-0.5	-4.3
455	GGTTCTGTCCCAGAGGACCT SEQ.ID.NO:940	-7.9	-29.6	83.3	-18.7	-3	-9.7
477	TGCGAGTATGGTTCCACTTC SEQ.ID.NO:941	-7.9	-25.3	73.3	-17.4	0	-5.8
792	CTCCTGAAGAAACCTTTACA SEQ.ID.NO:942	-7.9	-21.2	61.5	-13.3	0	-2.8
912	AACATTCCCATCTCTTTGCA SEQ.ID.NO:943	-7.9	-24.7	70.5	-16.8	0	-4.8
960	CTCAGTCGCTTAGATTTACA SEQ.ID.NO:944	-7.9	-22.3	66.9	-14.4	0	-3.1
1555	AAGCTTCTCTACTGCCTCTC SEQ.ID.NO:945	-7.9	-25.9	76.6	-18	0	-6.2
1571	CAAGAAGTGGCTCCTGAAGC SEQ.ID.NO:946	-7.9	-24	68.7	-14.7	-1.3	-4.8
1572	TCAAGAAGTGGCTCCTGAAG SEQ.ID.NO:947	-7.9	-22.6	66	-14.7	0	-3.7
1573	ATCAAGAAGTGGCTCCTGAA SEQ.ID.NO:948	-7.9	-22.6	65.8	-14.7	0	-3.7
1614	GGATTTTCAGGCTGGTGAAT SEQ.ID.NO:949	-7.9	-23.4	69	-15	-0.2	-5.4
1728	AGAAGTGGGGTAAACTTGTG SEQ.ID.NO:950	-7.9	-20.6	62.2	-11.7	-0.9	-4.1
1854	ATTTCTTGAGTGAAACTGGG SEQ.ID.NO:951	-7.9	-20.1	61.2	-11	-1.1	-5.5
1909	AATATTTACAGTTGTGGAAG SEQ.ID.NO:952	-7.9	-17.4	55.5	-9.5	0	-3.8
1929	AAAGTTGTTCTATCTAGCCC SEQ.ID.NO:953	-7.9	-23	68.2	-15.1	0	-3.7
2057	GATGAGCAAAATGAGATTTT SEQ.ID.NO:954	-7.9	-17.1	53.8	-8.3	-0.7	-4.1
152	TACCTCCTTGGATTGTTTTG SEQ.ID.NO:955	-7.8	-23.6	69.1	-15.1	-0.5	-4.6
864	CTTCGCATGTACATATCCAT SEQ.ID.NO:956	-7.8	-23.3	67.2	-15	0	-8
873	TGACACTTTCTTCGCATGTA SEQ.ID.NO:957	-7.8	-22.8	67.4	-15	0	-4.8
1011	CCTTCACTGTCTTCATTCAC SEQ.ID.NO:958	-7.8	-24.3	72.6	-16.5	0	-2.4
1281	TGGTCTTCATGGTCCAAAGT SEQ.ID.NO:959	-7.8	-24.2	71.2	-15.9	-0.1	-4.7
1643	GGCGACCCAGGAGACAGGCA SEQ.ID.NO:960	-7.8	-30.3	80.2	-22	-0.2	-4.2
1847	GAGTGAAACTGGGTACAAGT SEQ.ID.NO:961	-7.8	-20.8	62.5	-11.8	-1.1	-7

position	oligo	kcal/ mol total binding	kcal/ mol duplex formation	deg C Tm of Duplex	kcal/ mol target structure	kcal/ mol Intra-molecular oligo	kcal/ mol Inter-molecular oligo
1859	TCAAGATTTCTTGAGTGAAA SEQ.ID.NO:962	-7.8	-17.6	55.8	-7.9	-1.9	-10.3
1971	GAATGCAGGATTCCCTGGAG SEQ.ID.NO:963	-7.8	-25.4	71.3	-15.3	-2.3	-8.5
2007	AATCAATTTAATTAGGCAAA SEQ.ID.NO:964	-7.8	-15	49.2	-7.2	0	-4.1
2042	ATTTTCCCTAGTTCAACAGA SEQ.ID.NO:965	-7.8	-22.5	66.7	-14.7	0	-3.6
2103	CCAAGATTGAATACAACTCT SEQ.ID.NO:966	-7.8	-18.9	57	-9.8	-1.2	-4
114	AAGGCCCTGGGAGGATTCTG SEQ.ID.NO:967	-7.7	-27.4	75.9	-19.1	-0.1	-8.3
115	CAAGGCCCTGGGAGGATTCT SEQ.ID.NO:968	-7.7	-28.1	77.1	-19.6	-0.6	-7.6
301	GGTGGTCTTCAAAAAAAACT SEQ.ID.NO:969	-7.7	-17.5	54.1	-9.8	0	-2.6
752	TATAGTGGTATCCAGAGGCT SEQ.ID.NO:970	-7.7	-24.3	72.5	-16.1	-0.1	-4.1
931	AGTTAACAAGCATTCAGCCA SEQ.ID.NO:971	-7.7	-22.7	66.3	-14	-0.9	-8.7
1755	CATCACTGCACGTCCCAGAT SEQ.ID.NO:972	-7.7	-27.3	74.7	-19.6	0.4	-6.6
2064	ATGGTAAGATGAGCAAAATG SEQ.ID.NO:973	-7.7	-17	53.3	-9.3	0	-4.1
90	GAGTCTTCCTCTCCAGATCC SEQ.ID.NO:974	-7.6	-27.9	81.4	-19.6	-0.5	-5.5
234	AGGAAACTAAGAGAAGCAGT SEQ.ID.NO:975	-7.6	-18.7	57.5	-10.6	-0.2	-4.4
327	TTTCAATTGAAATGCACTTT SEQ.ID.NO:976	-7.6	-17.7	55.2	-8.2	-0.1	-11.9
478	TTGCGAGTATGGTTCCACTT SEQ.ID.NO:977	-7.6	-25	72	-17.4	0	-5.8
482	TGTATTGCGAGTATGGTTCC SEQ.ID.NO:978	-7.6	-24	70.5	-16.4	0	-4.1
490	AACATTGCTGTATTGCGAGT SEQ.ID.NO:979	-7.6	-22.4	65.6	-13.9	-0.7	-5
644	CTACCTCAGTTTCTCCCTGG SEQ.ID.NO:980	-7.6	-28	79.5	-19.9	-0.2	-4
1072	GGTGAGTTCAGTTTTCTCCC SEQ.ID.NO:981	-7.6	-26.6	79.6	-18.4	-0.3	-3.6
1904	TTACAGTTGTGGAAGTTACA SEQ.ID.NO:982	-7.6	-20.2	62.5	-12.6	0	-4.2
1996	TTAGGCAAACAGGGCTTGCC SEQ.ID.NO:983	-7.6	-26	72.5	-15	-3.4	-9.8
265	TTCATCTTGAGGAAATGTCC SEQ.ID.NO:984	-7.5	-21.2	63.8	-12.6	-1	-5.2
824	TACACTTGTACACAGCGTTT SEQ.ID.NO:985	-7.5	-22.5	66.4	-15	0	-6.3
825	TTACACTTGTACACAGCGTT SEQ.ID.NO:986	-7.5	-22.5	66.4	-15	0	-5.9
826	TTTACACTTGTACACAGCGT SEQ.ID.NO:987	-7.5	-22.5	66.4	-15	0	-6.3
1110	GAATCCATAATAAAATGTAG SEQ.ID.NO:988	-7.5	-14.5	48.1	-7	0	-2.7
1336	CTCAGCTGAACGAAGGAACA	-7.5	-21.5	61.8	-12.9	0	-10.1

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intramolecular oligo	kcal/mol Intermolecular oligo
	SEQ.ID.NO:989						
1342	GAAAATCTCAGCTGAACGAA SEQ.ID.NO:990	-7.5	-18.4	55.3	-9.8	0	-10.1
1346	TATTGAAAATCTCAGCTGAA SEQ.ID.NO:991	-7.5	-17.3	54.3	-8.1	-0.1	-11.6
1606	AGGCTGGTGAATCTTACACA SEQ.ID.NO:992	-7.5	-23.1	68.1	-14	-1.6	-5.4
1609	TTCAGGCTGGTGAATCTTAC SEQ.ID.NO:993	-7.5	-22.7	68.3	-14.7	-0.2	-5.2
1678	AGCGTGGTGATGATTGAATG SEQ.ID.NO:994	-7.5	-21.4	63	-13.9	0	-4.1
1922	TTCTATCTAGCCCAATATTT SEQ.ID.NO:995	-7.5	-21.8	64.8	-14.3	0	-4.1
2020	GAATTGAAGTAACAATCAAT SEQ.ID.NO:996	-7.5	-14.7	48.6	-5.5	-1.7	-6.1
2098	ATTGAATACAACTCTTTAAT SEQ.ID.NO:997	-7.5	-15.5	50.8	-7.1	-0.8	-4
199	TGTTTCTAAGTCTTCTTTTC SEQ.ID.NO:998	-7.4	-20.3	65.4	-12.3	-0.3	-2.7
202	CTATGTTTCTAAGTCTTCTT SEQ.ID.NO:999	-7.4	-20.3	64.5	-12.4	-0.1	-2.7
207	TTGAGCTATGTTTCTAAGTC SEQ.ID.NO:1000	-7.4	-20.4	64.3	-13	0	-5.1
232	GAAACTAAGAGAAGCAGTGT SEQ.ID.NO:1001	-7.4	-18.7	57.7	-11.3	0	-4.2
328	TTTTCAATTGAAATGCACTT SEQ.ID.NO:1002	-7.4	-17.7	55.2	-8.2	-0.4	-12.4
329	TTTTTCAATTGAAATGCACT SEQ.ID.NO:1003	-7.4	-17.7	55.2	-8.2	-0.4	-12.4
733	TCTGTCTCCACAAACAACAC SEQ.ID.NO:1004	-7.4	-21.7	63.5	-13.8	-0.1	-2.9
744	TATCCAGAGGCTCTGTCTCC SEQ.ID.NO:1005	-7.4	-27.5	80.5	-18.5	-1.5	-8
1012	ACCTTCACTGTCTTCATTCA SEQ.ID.NO:1006	-7.4	-24.3	72.6	-16.9	0	-2.6
1019	AGTCACGACCTTCACTGTCT SEQ.ID.NO:1007	-7.4	-25.8	74.7	-17.7	-0.5	-4.7
1935	GTAGAGAAAGTTGTTCTATC SEQ.ID.NO:1008	-7.4	-18.7	60.2	-9.8	-1.4	-4.5
2091	ACAACTCTTTAATAAAATAT SEQ.ID.NO:1009	-7.4	-13.1	45.7	-5.7	0	-3.7
183	TTTCTTCTTTCACTCCTTCT SEQ.ID.NO:1010	-7.3	-24	73.3	-16.7	0	0
198	GTTTCTAAGTCTTCTTTTCT SEQ.ID.NO:1011	-7.3	-21.2	67.8	-13.3	-0.3	-2.7
240	AAATCCAGGAAACTAAGAGA SEQ.ID.NO:1012	-7.3	-17.4	53.7	-9.5	-0.3	-5.7
306	TTTATGGTGGTCTTCAAAAA SEQ.ID.NO:1013	-7.3	-18.4	57.1	-11.1	0	-3.3
321	TTGAAATGCACTTTCTTTAT SEQ.ID.NO:1014	-7.3	-18.3	57.1	-9.4	-1.6	-9.2
322	ATTGAAATGCACTTTCTTTA SEQ.ID.NO:1015	-7.3	-18.3	57.1	-9.4	-1.6	-9.2
650	TCTCTGCTACCTCAGTTTCT SEQ.ID.NO:1016	-7.3	-25.9	77.8	-18.1	-0.2	-3.5

position	oligo	kcal/ mol total binding	kcal/ mol duplex forma- tion	deg C Tm of Duplex	kcal/ mol target struc- ture	kcal/ mol Intra- mole- cular oligo	kcal/ mol Inter- mole- cular oligo
863	TTCGCATGTACATATCCATC SEQ.ID.NO:1017	-7.3	-22.8	66.8	-15	0	-7.8
1381	TTCCAATAGGTCAGAATGCC SEQ.ID.NO:1018	-7.3	-23.4	67.5	-15	-1	-4.6
1567	AAGTGGCTCCTGAAGCTTCT SEQ.ID.NO:1019	-7.3	-25.7	74.2	-16.8	-1.3	-10.8
1636	CAGGAGACAGGCAAAGTGTT SEQ.ID.NO:1020	-7.3	-22.8	67	-15.5	0	-4
1658	TCCGTAATTCAGTCAGGCGA SEQ.ID.NO:1021	-7.3	-25.3	71.3	-18	0	-4
1891	AGTTACACATGTAATTACAA SEQ.ID.NO:1022	-7.3	-17	54.3	-8.5	-0.3	-10.3
74	ATCCCAGCGATTTTGCTACA SEQ.ID.NO:1023	-7.2	-25.9	71.8	-17.2	-1.4	-5.1
87	TCTTCCTCTCCAGATCCCAG SEQ.ID.NO:1024	-7.2	-28.8	81	-21.6	0	-4.5
158	GTCTTCTACCTCCTTGGATT SEQ.ID.NO:1025	-7.2	-26	76.1	-18.1	-0.5	-4.6
357	ATGAGATTCATTTTTGATCC SEQ.ID.NO:1026	-7.2	-19.8	61.2	-11.7	-0.8	-5.3
358	AATGAGATTCATTTTTGATC SEQ.ID.NO:1027	-7.2	-17.1	55.2	-8.3	-1.5	-6.9
379	GGTAGGTAAATGGGAATGTT SEQ.ID.NO:1028	-7.2	-20.4	61.6	-13.2	0	-2.5
959	TCAGTCGCTTAGATTTACAC SEQ.ID.NO:1029	-7.2	-21.6	65.5	-14.4	0	-3.1
1351	TTTCTTATTGAAAATCTCAG SEQ.ID.NO:1030	-7.2	-16.3	53.2	-8.1	-0.9	-4.1
1392	CGAATTCTTTCTTCCAATAG SEQ.ID.NO:1031	-7.2	-19.8	59.6	-11.8	-0.6	-6.4
1434	CTAAACATAGGTGTTATATA SEQ.ID.NO:1032	-7.2	-16.6	53.7	-7.7	-1.7	-5.9
1576	CACATCAAGAAGTGGCTCCT SEQ.ID.NO:1033	-7.2	-24.3	69.7	-16.6	-0.1	-5.1
1610	TTTCAGGCTGGTGAATCTTA SEQ.ID.NO:1034	-7.2	-22.6	68.1	-14.7	-0.5	-5.7
1638	CCCAGGAGACAGGCAAAGTG SEQ.ID.NO:1035	-7.2	-25.5	70.7	-18.3	0	-4
1839	CTGGGTACAAGTGAAATAAA SEQ.ID.NO:1036	-7.2	-17.1	53.4	-9.9	0	-5.2
1857	AAGATTTCTTGAGTGAAACT SEQ.ID.NO:1037	-7.2	-17.6	55.7	-9.4	-0.9	-5.7
1864	ATTCATCAAGATTTCTTGAG SEQ.ID.NO:1038	-7.2	-18.4	58.4	-9.3	-1.9	-10.7
2050	AAAATGAGATTTTCCCTAGT SEQ.ID.NO:1039	-7.2	-19.6	59.1	-11.5	-0.7	-5
2062	GGTAAGATGAGCAAAATGAG SEQ.ID.NO:1040	-7.2	-17.6	54.7	-10.4	0	-4.1
23	AGTCGGGGAGACAATGAGGT SEQ.ID.NO:1041	-7.1	-24.4	70.3	-15.2	-2.1	-5
53	ATGCTCAGAATCCAATTTCG SEQ.ID.NO:1042	-7.1	-21.5	62.6	-13.7	-0.4	-4
56	CAAATGCTCAGAATCCAATT SEQ.ID.NO:1043	-7.1	-19.5	57.9	-12.4	0	-2.9
229	ACTAAGAGAAGCAGTGTTCA	-7.1	-20.7	63.5	-12.9	-0.4	-6.8

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intra-molecular oligo	kcal/mol Inter-molecular oligo
	SEQ.ID.NO:1044 CTGAAGTTTCATCTTGAGGA						
272	SEQ.ID.NO:1045 TGGTAGGTAAATGGGAATGT	-7.1	-21.1	64.6	-14	0	-4.7
380	SEQ.ID.NO:1046 TCACGACCTTCACTGTCTTC	-7.1	-20.3	61.1	-13.2	0	-1.2
1017	SEQ.ID.NO:1047 CTACAAGAACCTGTACATGA	-7.1	-25.1	73	-17.3	-0.5	-3.7
1232	SEQ.ID.NO:1048 AATTCTACAAGAACCTGTAC	-7.1	-20.2	60	-13.1	0	-6.5
1236	SEQ.ID.NO:1049 TCAGCTGAACGAAGGAACAT	-7.1	-18.7	57.4	-10.6	-0.9	-5.5
1335	SEQ.ID.NO:1050 ATCTCAGCTGAACGAAGGAA	-7.1	-20.6	60	-12.6	0	-9.8
1338	SEQ.ID.NO:1051 TTGAAAATCTCAGCTGAACG	-7.1	-21	61.4	-12.8	0	-10.1
1344	SEQ.ID.NO:1052 TGTGGTCGTTTACTCTCCAT	-7.1	-18.6	56.1	-10.4	-0.1	-10.1
1712	SEQ.ID.NO:1053 AGACCCCTCCCCTGTAATCC	-7.1	-25.4	74.4	-17.6	-0.4	-3.9
1776	SEQ.ID.NO:1054 CAAGTGAAATAAAGGAAAGT	-7.1	-31.6	81.9	-24.5	0	-2.1
1832	SEQ.ID.NO:1055 AGGGCTTGCCAATTAGAATG	-7.1	-14.3	47.6	-7.2	0	-1.6
1986	SEQ.ID.NO:1056 TAGGCAAACAGGGCTTGCCA	-7.1	-22.7	65.4	-13.8	-1.8	-8.5
1995	SEQ.ID.NO:1057 ATACAACTCTTTAATAAAAT	-7.1	-26.6	73.2	-15	-4.5	-11.1
2093	SEQ.ID.NO:1058 AGCTATGTTTCTAAGTCTTC	-7.1	-13.1	45.7	-6	0	-3.7
204	SEQ.ID.NO:1059 AATCCAGGAAACTAAGAGAA	-7	-21.1	66.8	-14.1	0	-4.3
239	SEQ.ID.NO:1060 TGAACATTGCTGTATTGCGA	-7	-17.4	53.7	-9.9	-0.1	-5.7
492	SEQ.ID.NO:1061 CTTTTAAAATTTTATTTGTT	-7	-21.8	63.4	-13.9	-0.7	-5
1160	SEQ.ID.NO:1062 GCCATTTCCGTCAAAATGAG	-7	-14.3	48.8	-6.7	-0.2	-8
1206	SEQ.ID.NO:1063 TGCCATTTCCGTCAAAATGA	-7	-22.7	63.9	-14.1	-1.6	-6
1207	SEQ.ID.NO:1064 GTGAATTCTACAAGAACCTG	-7	-22.7	63.6	-14.1	-1.6	-6.2
1239	SEQ.ID.NO:1065 TGGACTTTCAAGGCCCTGGG	-7	-19.4	58.6	-11.7	-0.4	-7.1
123	SEQ.ID.NO:1066 TGGATTGTTTTGGGTCAGAG	-6.9	-27.8	76.4	-20.4	0	-7.8
144	SEQ.ID.NO:1067 AAACTAAGAGAAGCAGTGTT	-6.9	-22.7	68.9	-15.8	0	-3.4
231	SEQ.ID.NO:1068 CTCCAAAGTGTCTGAAGTTT	-6.9	-18.2	56.7	-11.3	0	-4.4
283	SEQ.ID.NO:1069 AATTGAAATGCACTTTCTTT	-6.9	-21.6	64.8	-14.7	0	-3
323	SEQ.ID.NO:1070 CATTTTTGATCCCATCCAAA	-6.9	-17.9	55.8	-9.4	-1.6	-9.2
349	SEQ.ID.NO:1071	-6.9	-22.5	63.8	-15	-0.3	-4.3

position	oligo	kcal/ mol total binding	kcal/ mol duplex forma-tion	deg C Tm of Duplex	kcal/ mol target struc-ture	kcal/ mol Intra-mole-cular oligo	kcal/ mol Inter-mole-cular oligo
454	GTTCTGTCCCAGAGGACCTG SEQ.ID.NO:1072	-6.9	-28.4	80.3	-19.2	-2.3	-6.5
706	ATCCCCTTTGATCCTCCCTG SEQ.ID.NO:1073	-6.9	-30.7	81.4	-23.8	0	-4.3
968	CATTTTTTCTCAGTCGCTTA SEQ.ID.NO:1074	-6.9	-22.5	68	-15.6	0	-3.1
1164	TCTTCTTTTAAAATTTTATT SEQ.ID.NO:1075	-6.9	-14.7	49.9	-7.3	0	-8
1231	TACAAGAACCTGTACATGAT SEQ.ID.NO:1076	-6.9	-19.3	58.2	-12.4	0	-6.5
1233	TCTACAAGAACCTGTACATG SEQ.ID.NO:1077	-6.9	-20	60.1	-13.1	0	-6.1
1332	GCTGAACGAAGGAACATAGC SEQ.ID.NO:1078	-6.9	-21	60.8	-14.1	0	-3.5
1423	TGTTATATATTCATCAGAGA SEQ.ID.NO:1079	-6.9	-17.9	57.7	-11	0	-3.9
1569	AGAAGTGGCTCCTGAAGCTT SEQ.ID.NO:1080	-6.9	-25	72.1	-16	-2.1	-7
1613	GATTTTCAGGCTGGTGAATC SEQ.ID.NO:1081	-6.9	-22.6	68	-15	-0.5	-5.7
1639	ACCCAGGAGACAGGCAAAGT SEQ.ID.NO:1082	-6.9	-25.7	71.4	-18.8	0	-4
1829	GTGAAATAAAGGAAAGTTAT SEQ.ID.NO:1083	-6.9	-14.1	47.5	-7.2	0	-2.7
1830	AGTGAAATAAAGGAAAGTTA SEQ.ID.NO:1084	-6.9	-14.1	47.6	-7.2	0	-2.6
1848	TGAGTGAAACTGGGTACAAG SEQ.ID.NO:1085	-6.9	-19.6	59.4	-11.5	-1.1	-7
2021	AGAATTGAAGTAACAATCAA SEQ.ID.NO:1086	-6.9	-14.7	48.7	-6.8	-0.9	-4.4
2053	AGCAAAATGAGATTTTCCCT SEQ.ID.NO:1087	-6.9	-21.2	61.7	-13.3	-0.9	-4.8
2065	TATGGTAAGATGAGCAAAAT SEQ.ID.NO:1088	-6.9	-16.7	52.8	-9.8	0	-4.1
2106	TTGCCAAGATTGAATACAAC SEQ.ID.NO:1089	-6.9	-18.6	56.2	-10.8	-0.8	-4.5
61	TGCTACAAATGCTCAGAATC SEQ.ID.NO:1090	-6.8	-20	60.2	-12.5	-0.4	-3.6
73	TCCCAGCGATTTTGCTACAA SEQ.ID.NO:1091	-6.8	-25.2	69.7	-16.8	-1.6	-6.1
116	TCAAGGCCCTGGGAGGATTC SEQ.ID.NO:1092	-6.8	-27.6	76.9	-20	-0.6	-8.3
367	GGAATGTTCAATGAGATTCA SEQ.ID.NO:1093	-6.8	-19.2	59.1	-11.7	-0.5	-7.6
972	TTCACATTTTTTCTCAGTCG SEQ.ID.NO:1094	-6.8	-21.4	65.6	-14.6	0	-2.5
1208	TTGCCATTTCCGTCAAAATG SEQ.ID.NO:1095	-6.8	-22.2	62.8	-14.1	-1.2	-6.2
1289	AAGCAATCTGGTCTTCATGG SEQ.ID.NO:1096	-6.8	-22.5	67	-15.7	0	-4.7
1390	AATTCTTTCTTCCAATAGGT SEQ.ID.NO:1097	-6.8	-20.8	63.4	-13.4	-0.3	-3.6
1542	GCCTCTCTATCCTTTATGTA SEQ.ID.NO:1098	-6.8	-25.1	74.2	-18.3	0	-2
1818	GAAAGTTATACATCAGATTA	-6.8	-16.3	53.1	-9.5	0	-3.4

position	oligo	kcal/ mol total binding	kcal/ mol duplex forma- tion	deg C Tm of Duplex	kcal/ mol target struc- ture	kcal/ mol Intra- mole- cular oligo	kcal/ mol Inter- mole- cular oligo
	SEQ.ID.NO:1099						
1910	CAATATTTACAGTTGTGGAA SEQ.ID.NO:1100	-6.8	-18.1	56.6	-11.3	0	-4.1
80	CTCCAGATCCCAGCGATTTT SEQ.ID.NO:1101	-6.7	-27.2	74.5	-20.5	0	-4.1
82	CTCTCCAGATCCCAGCGATT SEQ.ID.NO:1102	-6.7	-28.3	77.2	-21.6	0	-4.5
.159	TGTCTTCTACCTCCTTGGAT SEQ.ID.NO:1103	-6.7	-25.9	75.5	-18.5	-0.5	-5
342	GATCCCATCCAAATTTTTCA SEQ.ID.NO:1104	-6.7	-22.9	65.3	-16.2	0	-5.4
708	TCATCCCCTTTGATCCTCCC SEQ.ID.NO:1105	-6.7	-30.9	82.5	-24.2	0	-4.3
862	TCGCATGTACATATCCATCA SEQ.ID.NO:1106	-6.7	-23.4	67.6	-16.2	0	-8
1105	CATAATAAAATGTAGAAGAG SEQ.ID.NO:1107	-6.7	-12.7	44.8	-6	0	-2.4
1238	TGAATTCTACAAGAACCTGT SEQ.ID.NO:1108	-6.7	-19.4	58.6	-11.7	-0.9	-6.9
1240	TGTGAATTCTACAAGAACCT SEQ.ID.NO:1109	-6.7	-19.4	58.6	-11.7	-0.9	-8
1282	CTGGTCTTCATGGTCCAAAG SEQ.ID.NO:1110	-6.7	-23.9	69.8	-16.7	-0.2	-4.7
1361	CAGACGGAAGTTTCTTATTG SEQ.ID.NO:1111	-6.7	-20	60.7	-12.4	-0.8	-5.1
1530	TTTATGTATTGTCTATCTGG SEQ.ID.NO:1112	-6.7	-19.6	62.2	-12.9	0	-1.3
1738	GATTTCACAGAGAAGTGGGG SEQ.ID.NO:1113	-6.7	-22.1	66.2	-14.8	-0.3	-4.7
1739	AGATTTCACAGAGAAGTGGG SEQ.ID.NO:1114	-6.7	-20.9	63.7	-13.3	-0.7	-4.7
1958	CCTGGAGCCTTTTAAAACAC SEQ.ID.NO:1115	-6.7	-22.4	63.7	-15.7	0	-6.2
1994	AGGCAAACAGGGCTTGCCAA SEQ.ID.NO:1116	-6.7	-26.2	71.5	-15	-4.5	-11.1
2041	TTTTCCCTAGTTCAACAGAT SEQ.ID.NO:1117	-6.7	-22.5	66.7	-15.8	0	-3.6
2074	TATATGCAATATGGTAAGAT SEQ.ID.NO:1118	-6.7	-16.9	53.8	-9.5	-0.5	-5.6
2075	ATATATGCAATATGGTAAGA SEQ.ID.NO:1119	-6.7	-16.9	53.8	-9.5	-0.5	-5.6
2087	CTCTTTAATAAAATATATGC SEQ.ID.NO:1120	-6.7	-14.2	48.1	-7.5	0	-4.2
431	CTTGTTCTGTTAAAACACCA SEQ.ID.NO:1121	-6.6	-20.3	60.6	-12.8	-0.7	-5.5
432	ACTTGTTCTGTTAAAACACC SEQ.ID.NO:1122	-6.6	-19.8	60	-12.3	-0.7	-5.5
435	GCCACTTGTTCTGTTAAAAC SEQ.ID.NO:1123	-6.6	-21.4	63.5	-14.8	0	-3.3
469	TGGTTCCACTTCCAGGTTCT SEQ.ID.NO:1124	-6.6	-27.7	80.3	-20.5	-0.3	-4.8
598	GAGTTCATATATTCCAGGAG SEQ.ID.NO:1125	-6.6	-21.4	65.5	-14.8	0	-5.3
753	TTATAGTGGTATCCAGAGGC SEQ.ID.NO:1126	-6.6	-23.5	70.8	-16.1	-0.6	-6.9

position	oligo	kcal/ mol total binding	kcal/ mol duplex forma- tion	deg C Tm of Duplex	kcal/ mol target struc- ture	kcal/ mol Intra- mole- cular oligo	kcal/ mol Inter- mole- cular oligo
928	TAACAAGCATTCAGCCAACA SEQ.ID.NO:1127	-6.6	-21.6	62.3	-14	-0.9	-4.1
1036	CGAGGTCACTTGTCGCAAGT SEQ.ID.NO:1128	-6.6	-25.5	72.3	-16.9	-2	-10.6
1093	TAGAAGAGTCTGTTGATCTG SEQ.ID.NO:1129	-6.6	-19.9	62.7	-12.8	-0.2	-5.8
1109	AATCCATAATAAAATGTAGA SEQ.ID.NO:1130	-6.6	-14.5	48.1	-7.9	0	-2.8
1843	GAAACTGGGTACAAGTGAAA SEQ.ID.NO:1131	-6.6	-18.2	55.6	-11.6	0	-6
2088	ACTCTTTAATAAAATATATG SEQ.ID.NO:1132	-6.6	-12.6	44.9	-6	0	-4.2
55	AAATGCTCAGAATCCAATTT SEQ.ID.NO:1133	-6.5	-18.9	57	-12.4	0	-3.6
153	CTACCTCCTTGGATTGTTTT SEQ.ID.NO:1134	-6.5	-24.5	71.2	-17.3	-0.5	-4.4
172	ACTCCTTCTACGATGTCTTC SEQ.ID.NO:1135	-6.5	-24.1	71.4	-17.6	0	-3.5
330	ATTTTTCAATTGAAATGCAC SEQ.ID.NO:1136	-6.5	-16.8	53.3	-8.2	-0.4	-12.4
483	CTGTATTGCGAGTATGGTTC SEQ.ID.NO:1137	-6.5	-22.9	68.7	-16.4	0	-4.1
802	GGTAATGCTTCTCCTGAAGA SEQ.ID.NO:1138	-6.5	-23.3	68.3	-14.6	-2.2	-6.7
1005	CTGTCTTCATTCACGGTCTG SEQ.ID.NO:1139	-6.5	-24.5	72.6	-18	0	-3.5
1007	CACTGTCTTCATTCACGGTC SEQ.ID.NO:1140	-6.5	-24.5	72.5	-18	0	-3.5
1018	GTCACGACCTTCACTGTCTT SEQ.ID.NO:1141	-6.5	-25.9	74.7	-19.4	0	-3.7
1020	AAGTCACGACCTTCACTGTC SEQ.ID.NO:1142	-6.5	-24.2	70.2	-17.7	0	-4.7
1079	GATCTGGGGTGAGTTCAGTT SEQ.ID.NO:1143	-6.5	-25	75.9	-18	-0.2	-4.1
1096	ATGTAGAAGAGTCTGTTGAT SEQ.ID.NO:1144	-6.5	-19.8	62.4	-12.8	-0.2	-5.8
1245	TTTTTGTGAATTCTACAAG SEQ.ID.NO:1145	-6.5	-16.9	54.6	-9	-0.7	-10.5
1477	CTCCTCTTGAGTCATTTTCA SEQ.ID.NO:1146	-6.5	-23.9	72.2	-16.9	-0.2	-5.8
1623	AAGTGTTGAGGATTTTCAGG SEQ.ID.NO:1147	-6.5	-20.8	64.2	-14.3	0	-3.2
1631	GACAGGCAAAGTGTTGAGGA SEQ.ID.NO:1148	-6.5	-22.7	66.8	-15.3	-0.7	-3.9
1785	AAAGGAGCTAGACCCCTCCC SEQ.ID.NO:1149	-6.5	-28.9	76.6	-20.4	-2	-7.6
1808	CATCAGATTAATATGAGAGA SEQ.ID.NO:1150	-6.5	-17	54.5	-10.5	0	-7
1831	AAGTGAAATAAAGGAAAGTT SEQ.ID.NO:1151	-6.5	-13.7	46.6	-7.2	0	-2.3
1889	TTACACATGTAATTACAACA SEQ.ID.NO:1152	-6.5	-16.7	53.1	-9	-0.2	-10.3
113	AGGCCCTGGGAGGATTCTGG SEQ.ID.NO:1153	-6.4	-29.3	81	-22.1	-0.6	-8.3
324	CAATTGAAATGCACTTTCTT	-6.4	-18.5	56.7	-11.1	-0.9	-8.5

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intramolecular oligo	kcal/mol Intermolecular oligo
	SEQ.ID.NO:1154 GTAGGTAAATGGGAATGTTC						
378	SEQ.ID.NO:1155 GGTAGAGAGTCTCAGCTGGC	-6.4	-19.6	60.4	-13.2	0	-4.5
626	SEQ.ID.NO:1156 TTTTACACTTGTACACAGCG	-6.4	-26.6	80.6	-18.8	-1.1	-10
827	SEQ.ID.NO:1157 TCGCAAGTCACGACCTTCAC	-6.4	-21.4	63.6	-15	0	-6.3
1024	SEQ.ID.NO:1158 CAAAGTCTGAAATCCTGGTA	-6.4	-25.4	70.5	-18.3	-0.5	-4.7
1267	SEQ.ID.NO:1159 GCAATCTGGTCTTCATGGTC	-6.4	-20.4	60.7	-14	0	-4.6
1287	SEQ.ID.NO:1160 AGAGCATACTCCTCTTGAGT	-6.4	-24.8	74.4	-18.4	0	-4.7
1485	SEQ.ID.NO:1161 ACATCAAGAAGTGGCTCCTG	-6.4	-24.4	73	-16.4	-1.5	-7.1
1575	SEQ.ID.NO:1162 GGCTGGTGAATCTTACACAA	-6.4	-23.6	68.4	-17.2	0	-3.7
1605	SEQ.ID.NO:1163 GCGACCCAGGAGACAGGCAA	-6.4	-22.4	65.6	-15.1	-0.8	-5.9
1642	SEQ.ID.NO:1164 CGTCCCAGATTTCACAGAGA	-6.4	-28.4	75.4	-22	0	-4.2
1745	SEQ.ID.NO:1165 AAAAAGGAGCTAGACCCCTC	-6.4	-25.1	71.1	-18.7	0	-2.7
1787	SEQ.ID.NO:1166 AAGGAAAGTTATACATCAGA	-6.4	-23.5	65.7	-16.6	-0.2	-5.3
1821	SEQ.ID.NO:1167 AATACAACTCTTTAATAAAA	-6.4	-17	54.2	-10.6	0	-2.9
2094	SEQ.ID.NO:1168 TTATTGCCAAGATTGAATAC	-6.4	-12.4	44.2	-6	0	-3.7
2109	SEQ.ID.NO:1169 ACAAATGCTCAGAATCCAAT	-6.4	-18.2	56.1	-11.8	0	-3.7
57	SEQ.ID.NO:1170 TCCAGATCCCAGCGATTTTG	-6.3	-19.6	58.1	-13.3	0	-3.6
79	SEQ.ID.NO:1171 TCCTTCTACGATGTCTTCTA	-6.3	-26.3	72.5	-20	0	-4.5
170	SEQ.ID.NO:1172 CACTCCTTCTACGATGTCTT	-6.3	-23.6	70.2	-17.3	0	-3.5
173	SEQ.ID.NO:1173 GTCTCAGCTGGCATACGCCT	-6.3	-24.4	70.9	-18.1	0	-3.5
618	SEQ.ID.NO:1174 CCTTTACACCCCTCACAGGT	-6.3	-29.4	81.7	-20.2	-2.9	-9.9
780	SEQ.ID.NO:1175 GAGGTCACTTGTCGCAAGTC	-6.3	-29.2	79	-22.2	-0.5	-3.9
1035	SEQ.ID.NO:1176 TTCTACAAGAACCTGTACAT	-6.3	-25.1	74.1	-16.6	-2.2	-10.8
1234	SEQ.ID.NO:1177 GTTTCTTATTGAAAATCTCA	-6.3	-20.1	60.5	-13.1	-0.4	-6.9
1352	SEQ.ID.NO:1178 GAATTCTTTCTTCCAATAGG	-6.3	-17.5	55.9	-9.7	-1.4	-4.5
1391	SEQ.ID.NO:1179 ACTAAACATAGGTGTTATAT	-6.3	-20.2	61.6	-13.4	-0.1	-6.1
1435	SEQ.ID.NO:1180 TCTTGAGTCATTTTCAGTTC	-6.3	-17.1	54.8	-9.1	-1.7	-5.8
1473	SEQ.ID.NO:1181	-6.3	-21.4	68.2	-15.1	0	-5.8

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intra-molecular oligo	kcal/mol Inter-molecular oligo
1548	TCTACTGCCTCTCTATCCTT SEQ.ID.NO:1182	-6.3	-26.5	77.4	-20.2	0	-3
1577	GCACATCAAGAAGTGGCTCC SEQ.ID.NO:1183	-6.3	-25.2	72	-18	-0.8	-6.4
1693	TGACATCAGCATCTCAGCGT SEQ.ID.NO:1184	-6.3	-25.3	73.2	-18	-0.9	-4.1
2105	TGCCAAGATTGAATACAACT SEQ.ID.NO:1185	-6.3	-19.4	57.7	-12.2	-0.8	-4.5
2113	TGCTTTATTGCCAAGATTGA SEQ.ID.NO:1186	-6.3	-21.8	64.1	-15.5	0	-3.7
24	AAGTCGGGGAGACAATGAGG SEQ.ID.NO:1187	-6.2	-22.5	64.9	-14.2	-2.1	-4.8
104	GAGGATTCTGGACTGAGTCT SEQ.ID.NO:1188	-6.2	-23.8	71.8	-16.3	-1.2	-6.2
147	CCTTGGATTGTTTTGGGTCA SEQ.ID.NO:1189	-6.2	-25.1	73.2	-18.9	0	-2.7
266	TTTCATCTTGAGGAAATGTC SEQ.ID.NO:1190	-6.2	-19.3	60.3	-12.6	-0.2	-7.1
620	GAGTCTCAGCTGGCATACGC SEQ.ID.NO:1191	-6.2	-27.1	77.8	-20	-0.4	-9.6
642	ACCTCAGTTTCTCCCTGGTA SEQ.ID.NO:1192	-6.2	-28.3	81.1	-21.6	-0.2	-4.7
745	GTATCCAGAGGCTCTGTCTC SEQ.ID.NO:1193	-6.2	-26.7	80.6	-19.4	-1	-7.5
930	GTTAACAAGCATTCAGCCAA SEQ.ID.NO:1194	-6.2	-22	63.9	-14.8	-0.9	-8
1037	TCGAGGTCACTTGTCGCAAG SEQ.ID.NO:1195	-6.2	-24.7	70.6	-17.1	-1.3	-9.2
1612	ATTTTCAGGCTGGTGAATCT SEQ.ID.NO:1196	-6.2	-22.9	68.6	-16	-0.5	-5.7
1709	GGTCGTTTACTCTCCATGAC SEQ.ID.NO:1197	-6.2	-25	73	-18.8	0	-4.5
1911	CCAATATTTACAGTTGTGGA SEQ.ID.NO:1198	-6.2	-20.8	62.4	-14.6	0	-4.1
2026	CAGATAGAATTGAAGTAACA SEQ.ID.NO:1199	-6.2	-16	51.7	-9.8	0	-3.1
2095	GAATACAACTCTTTAATAAA SEQ.ID.NO:1200	-6.2	-13.7	46.8	-7.5	0	-3.4
162	CGATGTCTTCTACCTCCTTG SEQ.ID.NO:1201	-6.1	-25.5	72.7	-19.4	0	-3
278	AAGTGTCTGAAGTTTCATCT SEQ.ID.NO:1202	-6.1	-20.7	64.7	-14.6	0	-4.7
284	ACTCCAAAGTGTCTGAAGTT SEQ.ID.NO:1203	-6.1	-21.7	65	-15.6	0	-4.7
430	TTGTTCTGTTAAAACACCAA SEQ.ID.NO:1204	-6.1	-18.7	56.9	-11.7	-0.7	-5.5
471	TATGGTTCCACTTCCAGGTT SEQ.ID.NO:1205	-6.1	-26.1	75.7	-19.1	-0.7	-5.6
649	CTCTGCTACCTCAGTTTCTC SEQ.ID.NO:1206	-6.1	-25.9	77.8	-19.3	-0.2	-3.6
822	CACTTGTACACAGCGTTTTT SEQ.ID.NO:1207	-6.1	-22.8	67.1	-16.7	0	-6.3
870	CACTTTCTTCGCATGTACAT SEQ.ID.NO:1208	-6.1	-22.9	67.3	-16.3	0	-7.6
1023	CGCAAGTCACGACCTTCACT	-6.1	-25.9	70.9	-19.8	0	-3.9

position	oligo	kcal/ mol total binding	kcal/ mol duplex forma- tion	deg C Tm of Duplex	kcal/ mol target struc- ture	kcal/ mol Intra- mole- cular oligo	kcal/ mol Inter- mole- cular oligo
	SEQ.ID.NO:1209						
	AGCAATCTGGTCTTCATGGT						
1288	SEQ.ID.NO:1210	-6.1	-24.4	72.9	-18.3	0	-4.7
	ATACTCCTCTTGAGTCATTT						
1480	SEQ.ID.NO:1211	-6.1	-22.6	68.9	-14.8	-1.7	-5.8
	AAGCAGAGCATACTCCTCTT						
1489	SEQ.ID.NO:1212	-6.1	-24.4	71.4	-17.4	-0.8	-6.3
	TATGTATTGTCTATCTGGAG						
1528	SEQ.ID.NO:1213	-6.1	-20	63.2	-13.9	0	-3
	AATCCCCATCACTGCACGTC						
1761	SEQ.ID.NO:1214	-6.1	-27.7	74.8	-21.6	0	-4.8
	ACAAGTGAAATAAAGGAAAG						
1833	SEQ.ID.NO:1215	-6.1	-13.3	45.6	-7.2	0	-2.5
	TAGAATTGAAGTAACAATCA						
2022	SEQ.ID.NO:1216	-6.1	-15.1	49.8	-8	-0.9	-4.4
	GTCGGGGAGACAATGAGGTG						
22	SEQ.ID.NO:1217	-6	-24.4	69.9	-17	-1.3	-4.7
	TTGGATTGTTTTGGGTCAGA						
145	SEQ.ID.NO:1218	-6	-22.8	69	-16.8	0	-3.4
	TGAAATGCACTTTCTTTATG						
320	SEQ.ID.NO:1219	-6	-18.2	56.7	-10.6	-1.6	-9.2
	TGATCCCATCCAAATTTTTC						
343	SEQ.ID.NO:1220	-6	-22.2	64.1	-16.2	0	-5.4
	GTTCCACTTCCAGGTTCTGT						
467	SEQ.ID.NO:1221	-6	-27.7	81.3	-21.2	-0.2	-3.8
	GGCATCTCTGCTACCTCAGT						
654	SEQ.ID.NO:1222	-6	-28.1	81.6	-19.9	-2.2	-7.8
	GTCGCAAGTCACGACCTTCA						
1025	SEQ.ID.NO:1223	-6	-26.4	73.2	-18.3	-2.1	-6.8
	CTGAACGAAGGAACATAGCT						
1331	SEQ.ID.NO:1224	-6	-20.1	58.8	-14.1	0	-4.4
	CAGCTGAACGAAGGAACATA						
1334	SEQ.ID.NO:1225	-6	-19.9	58.2	-13.4	0	-7.6
	CTATTTCGAATTCTTTCTTC						
1398	SEQ.ID.NO:1226	-6	-19.3	60.3	-12.5	-0.6	-6.7
	CAGAGCATACTCCTCTTGAG						
1486	SEQ.ID.NO:1227	-6	-23.9	70.6	-16.4	-1.4	-6.9
	CTTTATGTATTGTCTATCTG						
1531	SEQ.ID.NO:1228	-6	-19.3	61.6	-13.3	0	-0.9
	GAATGTCCGTAATTCAGTCA						
1663	SEQ.ID.NO:1229	-6	-22	65	-15.1	-0.7	-4.6
	TGGTCGTTTACTCTCCATGA						
1710	SEQ.ID.NO:1230	-6	-24.8	72.2	-18.8	0	-4.5
	TTGAGTGAAACTGGGTACAA						
1849	SEQ.ID.NO:1231	-6	-19.7	59.5	-12.5	-1.1	-6.3
	AAGATTGAATACAACTCTTT						
2101	SEQ.ID.NO:1232	-6	-16.4	52.7	-8.5	-1.9	-5.4
	GATCCCAGCGATTTTGCTAC						
75	SEQ.ID.NO:1233	-5.9	-25.8	72	-18.3	-1.6	-6.5
	GACTTTCAAGGCCCTGGGAG						
121	SEQ.ID.NO:1234	-5.9	-27.2	75.6	-20.8	0	-8.3
	TTTGGGTCAGAGATGGACTT						
136	SEQ.ID.NO:1235	-5.9	-23.1	69.3	-16.6	-0.3	-5.3
	TCTTCTACCTCCTTGGATTG						
157	SEQ.ID.NO:1236	-5.9	-24.8	72.4	-18.2	-0.5	-4.6

position	oligo	kcal/ mol total binding	kcal/ mol duplex formation	deg C Tm of Duplex	kcal/ mol target structure	kcal/ mol Intra-molecular oligo	kcal/ mol Inter-molecular oligo
345	TTTGATCCCATCCAAATTTT SEQ.ID.NO:1237	-5.9	-21.9	63	-15.5	-0.2	-5.4
347	TTTTTGATCCCATCCAAATT SEQ.ID.NO:1238	-5.9	-21.9	63	-15.3	-0.5	-3.8
476	GCGAGTATGGTTCCACTTCC SEQ.ID.NO:1239	-5.9	-27.3	77.1	-21.4	0	-5.6
496	AAACTGAACATTGCTGTATT SEQ.ID.NO:1240	-5.9	-18.3	56.3	-11.7	-0.5	-3.9
564	GGCTGCTGGGGGTAGAAACC SEQ.ID.NO:1241	-5.9	-27.7	76.5	-20.5	-1.2	-8.5
627	TGGTAGAGAGTCTCAGCTGG SEQ.ID.NO:1242	-5.9	-24.8	75.4	-18.1	-0.3	-9.2
781	ACCTTTACACCCCTCACAGG SEQ.ID.NO:1243	-5.9	-28.2	76.3	-21.8	-0.2	-3.6
796	GCTTCTCCTGAAGAAACCTT SEQ.ID.NO:1244	-5.9	-23.7	67.5	-15.6	-2.2	-5.7
932	CAGTTAACAAGCATTCAGCC SEQ.ID.NO:1245	-5.9	-22.7	66.3	-15.8	-0.9	-8.7
1479	TACTCCTCTTGAGTCATTTT SEQ.ID.NO:1246	-5.9	-22.7	69.3	-15.1	-1.7	-5.8
1509	GACAGGATAACAATTGCTGT SEQ.ID.NO:1247	-5.9	-20.5	61.3	-13.2	-1.3	-8.5
1532	CCTTTATGTATTGTCTATCT SEQ.ID.NO:1248	-5.9	-21.3	65.7	-15.4	0	-0.9
1574	CATCAAGAAGTGGCTCCTGA SEQ.ID.NO:1249	-5.9	-24	69.1	-18.1	0	-3.7
1991	CAAACAGGGCTTGCCAATTA SEQ.ID.NO:1250	-5.9	-23	64.8	-15.3	-1.8	-8.5
2001	TTTAATTAGGCAAACAGGGC SEQ.ID.NO:1251	-5.9	-20.4	60.8	-14.5	0	-6.9
2006	ATCAATTTAATTAGGCAAAC SEQ.ID.NO:1252	-5.9	-15.9	51.3	-10	0	-4.1
2089	AACTCTTTAATAAAATATAT SEQ.ID.NO:1253	-5.9	-11.9	43.4	-6	0	-3.9
2110	TTTATTGCCAAGATTGAATA SEQ.ID.NO:1254	-5.9	-18.1	55.9	-12.2	0	-3.7
89	AGTCTTCCTCTCCAGATCCC SEQ.ID.NO:1255	-5.8	-29.3	83.7	-23.5	0	-4.5
434	CCACTTGTTCTGTTAAAACA SEQ.ID.NO:1256	-5.8	-20.3	60.6	-14	-0.2	-5.4
819	TTGTACACAGCGTTTTTGGT SEQ.ID.NO:1257	-5.8	-23.4	69.2	-17.6	0	-6.2
935	TTTCAGTTAACAAGCATTCA SEQ.ID.NO:1258	-5.8	-19.5	60.3	-13.7	0	-6.5
1151	TTTTATTTGTTATTTCCTGA SEQ.ID.NO:1259	-5.8	-19.3	60.6	-13.5	0	-1.7
1834	TACAAGTGAAATAAAGGAAA SEQ.ID.NO:1260	-5.8	-13	45	-7.2	0	-2.4
1905	TTTACAGTTGTGGAAGTTAC SEQ.ID.NO:1261	-5.8	-19.6	61.6	-13.8	0	-3.4
1921	TCTATCTAGCCCAATATTTA SEQ.ID.NO:1262	-5.8	-21.4	63.9	-15.6	0	-4.1
565	AGGCTGCTGGGGGTAGAAAC SEQ.ID.NO:1263	-5.7	-25.7	73.3	-20	0	-6.1
1317	ATAGCTTCAACCGCAGACCC	-5.7	-27.2	73.3	-20.8	-0.5	-4.6

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intra-molecular oligo	kcal/mol Inter-molecular oligo
	SEQ.ID.NO:1264						
	CCATCACTGCACGTCCCAGA						
1756	SEQ.ID.NO:1265	-5.7	-29.3	78.1	-22.9	-0.5	-7.5
	ACAGATAGAATTGAAGTAAC						
2027	SEQ.ID.NO:1266	-5.7	-15.5	50.9	-9.8	0	-3.1
	ATATGGTAAGATGAGCAAAA						
2066	SEQ.ID.NO:1267	-5.7	-16.7	52.8	-11	0	-4.1
	TACAACTCTTTAATAAAATA						
2092	SEQ.ID.NO:1268	-5.7	-12.8	45.1	-7.1	0	-3.7
	TCTGAAGTTTCATCTTGAGG						
273	SEQ.ID.NO:1269	-5.6	-20.9	64.7	-15.3	0	-4.7
	TTCCACTTCCAGGTTCTGTC						
466	SEQ.ID.NO:1270	-5.6	-26.9	79.4	-20.8	-0.2	-3.8
	ATCTCTGCTACCTCAGTTTC						
651	SEQ.ID.NO:1271	-5.6	-25	75.6	-18.9	-0.2	-3.6
	CAGGCATCTCTGCTACCTCA						
656	SEQ.ID.NO:1272	-5.6	-27.6	79	-19.8	-2.2	-5.6
	CTGTCTCCACAAACAACACA						
732	SEQ.ID.NO:1273	-5.6	-22	63.2	-15.9	-0.1	-2.9
	ATTTCAGTTAACAAGCATTC						
936	SEQ.ID.NO:1274	-5.6	-18.8	59	-13.2	0	-7.3
	ATTTTTTCTCAGTCGCTTAG						
967	SEQ.ID.NO:1275	-5.6	-21.8	67.1	-16.2	0	-3.1
	TCTGTTGATCTGGGGTGAGT						
1085	SEQ.ID.NO:1276	-5.6	-25.1	75.7	-19.5	0	-4.9
	GTCTGTTGATCTGGGGTGAG						
1086	SEQ.ID.NO:1277	-5.6	-25.1	75.7	-19.5	0	-4.9
	CCACTATTTCGAATTCTTTC						
1401	SEQ.ID.NO:1278	-5.6	-20.8	62.2	-15.2	0	-6.7
	AGACAGGATAACAATTGCTG						
1510	SEQ.ID.NO:1279	-5.6	-19.3	58.5	-13.2	-0.2	-7
	CAAAATGAGATTTTCCCTAG						
2051	SEQ.ID.NO:1280	-5.6	-19.1	57.4	-12.5	-0.9	-4.8
	ATGAGCAAAATGAGATTTTC						
2056	SEQ.ID.NO:1281	-5.6	-16.9	53.7	-10.3	-0.9	-4.8
	TATGCAATATGGTAAGATGA						
2072	SEQ.ID.NO:1282	-5.6	-17.8	55.6	-12.2	0	-5.6
	ATGTCTTCTACCTCCTTGGA						
160	SEQ.ID.NO:1283	-5.5	-25.9	75.5	-19.7	-0.5	-4.3
	TTGATCCCATCCAAATTTTT						
344	SEQ.ID.NO:1284	-5.5	-21.9	63	-16.4	0	-5.4
	TTTTGATCCCATCCAAATTT						
346	SEQ.ID.NO:1285	-5.5	-21.9	63	-15.7	-0.5	-4.3
	ATGGTTCCACTTCCAGGTTC						
470	SEQ.ID.NO:1286	-5.5	-26.8	78.1	-20.4	-0.7	-5.6
	GAACATTGCTGTATTGCGAG						
491	SEQ.ID.NO:1287	-5.5	-21.8	63.8	-15.4	-0.7	-5
	GGAAATCTGTGGTTGAACTT						
520	SEQ.ID.NO:1288	-5.5	-20.5	61.7	-15	0	-3.4
	CCCTGGTAGAGAGTCTCAGC						
630	SEQ.ID.NO:1289	-5.5	-27.6	80.6	-20.7	-1.1	-10
	ACTTTCTTCGCATGTACATA						
869	SEQ.ID.NO:1290	-5.5	-21.9	65.5	-15.9	0	-8
	CAAGCATTCAGCCAACATTC						
925	SEQ.ID.NO:1291	-5.5	-22.9	66.1	-16.4	-0.9	-4.1

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intra-molecular oligo	kcal/mol Inter-molecular oligo
1116	TTATATGAATCCATAATAAA SEQ.ID.NO:1292	-5.5	-13.8	46.8	-7.2	-1	-3.9
1315	AGCTTCAACCGCAGACCCTT SEQ.ID.NO:1293	-5.5	-28.5	76	-22.3	-0.5	-4.3
1422	GTTATATATTCATCAGAGAT SEQ.ID.NO:1294	-5.5	-17.9	57.8	-12.4	0	-3.9
1748	GCACGTCCCAGATTTCACAG SEQ.ID.NO:1295	-5.5	-26.6	74.1	-21.1	0	-4.6
1970	AATGCAGGATTCCCTGGAGC SEQ.ID.NO:1296	-5.5	-26.6	74.2	-18.1	-3	-8.7
2090	CAACTCTTTAATAAAATATA SEQ.ID.NO:1297	-5.5	-12.6	44.7	-7.1	0	-3.7
276	GTGTCTGAAGTTTCATCTTG SEQ.ID.NO:1298	-5.4	-21.5	67.1	-16.1	0	-4.5
341	ATCCCATCCAAATTTTTCAA SEQ.ID.NO:1299	-5.4	-21.6	62.1	-16.2	0	-4.6
356	TGAGATTCATTTTTGATCCC SEQ.ID.NO:1300	-5.4	-21.8	65.1	-15.5	-0.8	-4.5
468	GGTTCCACTTCCAGGTTCTG SEQ.ID.NO:1301	-5.4	-27.7	80.3	-22.3	0	-3.6
791	TCCTGAAGAAACCTTTACAC SEQ.ID.NO:1302	-5.4	-20.5	60.2	-15.1	0	-2.8
1237	GAATTCTACAAGAACCTGTA SEQ.ID.NO:1303	-5.4	-19.1	58.1	-12.7	-0.9	-6.8
1436	AACTAAACATAGGTGTTATA SEQ.ID.NO:1304	-5.4	-16.4	52.9	-9.7	-1.2	-5.3
1568	GAAGTGGCTCCTGAAGCTTC SEQ.ID.NO:1305	-5.4	-25.4	73.5	-17.9	-2.1	-9.8
1740	CAGATTTCACAGAGAAGTGG SEQ.ID.NO:1306	-5.4	-20.4	62.3	-14.1	-0.7	-4.6
1749	TGCACGTCCCAGATTTCACA SEQ.ID.NO:1307	-5.4	-26.6	73.6	-21.2	0	-4.7
1760	ATCCCCATCACTGCACGTCC SEQ.ID.NO:1308	-5.4	-30.4	80.5	-25	0	-4.8
1865	TATTCATCAAGATTTCTTGA SEQ.ID.NO:1309	-5.4	-18.1	57.7	-10.5	-2.2	-10.9
2112	GCTTTATTGCCAAGATTGAA SEQ.ID.NO:1310	-5.4	-21.1	62.2	-15.7	0	-3.7
230	AACTAAGAGAAGCAGTGTTC SEQ.ID.NO:1311	-5.3	-19.3	60	-14	0	-5.5
305	TTATGGTGGTCTTCAAAAAA SEQ.ID.NO:1312	-5.3	-17.6	55	-12.3	0	-3.3
715	ACACAGCTCATCCCCTTTGA SEQ.ID.NO:1313	-5.3	-27.7	76.7	-22.4	0	-4.4
823	ACACTTGTACACAGCGTTTT SEQ.ID.NO:1314	-5.3	-22.9	67.3	-17.6	0	-6.3
1084	CTGTTGATCTGGGGTGAGTT SEQ.ID.NO:1315	-5.3	-24.8	74.3	-19.5	0	-4.2
1097	AATGTAGAAGAGTCTGTTGA SEQ.ID.NO:1316	-5.3	-19.1	60.2	-13.8	0.1	-5.8
1611	TTTTCAGGCTGGTGAATCTT SEQ.ID.NO:1317	-5.3	-23	69	-17	-0.5	-5.7
1729	GAGAAGTGGGGTAAACTTGT SEQ.ID.NO:1318	-5.3	-21.2	63.6	-14.9	-0.9	-4.1
137	TTTTGGGTCAGAGATGGACT	-5.2	-23.1	69.3	-16.7	-1.1	-5.3

position	oligo	kcal/ mol total binding	kcal/ mol duplex forma- tion	deg C Tm of Duplex	kcal/ mol target struc- ture	kcal/ mol Intra- mole- cular oligo	kcal/ mol Inter- mole- cular oligo
	SEQ.ID.NO:1319						
208	TTTGAGCTATGTTTCTAAGT SEQ.ID.NO:1320	-5.2	-20.1	63.1	-14.9	0	-5.1
433	CACTTGTTCTGTTAAAACAC SEQ.ID.NO:1321	-5.2	-18.5	57.5	-12.4	-0.7	-5.5
587	TTCCAGGAGAGTACCACTCT SEQ.ID.NO:1322	-5.2	-25.8	74.9	-18.1	-2.5	-9.1
872	GACACTTTCTTCGCATGTAC SEQ.ID.NO:1323	-5.2	-23	68.1	-17.8	0	-4.8
955	TCGCTTAGATTTACACTGAA SEQ.ID.NO:1324	-5.2	-20.1	60.5	-14.9	0	-3.1
1081	TTGATCTGGGGTGAGTTCAG SEQ.ID.NO:1325	-5.2	-23.8	72	-18.6	0	-4.9
1104	ATAATAAAATGTAGAAGAGT SEQ.ID.NO:1326	-5.2	-13.2	46	-8	0	-1.2
1360	AGACGGAAGTTTCTTATTGA SEQ.ID.NO:1327	-5.2	-19.9	60.7	-13.8	-0.8	-5.7
1607	CAGGCTGGTGAATCTTACAC SEQ.ID.NO:1328	-5.2	-23.1	68.1	-17.2	-0.5	-4.9
1608	TCAGGCTGGTGAATCTTACA SEQ.ID.NO:1329	-5.2	-23.3	69.1	-18.1	0	-4.3
1992	GCAAACAGGGCTTGCCAATT SEQ.ID.NO:1330	-5.2	-25.1	69.2	-18.1	-1.8	-8.5
2005	TCAATTTAATTAGGCAAACA SEQ.ID.NO:1331	-5.2	-16.6	52.6	-11.4	0	-4.1
54	AATGCTCAGAATCCAATTTC SEQ.ID.NO:1332	-5.1	-20	60.2	-14.9	0	-3.6
197	TTTCTAAGTCTTCTTTTCTT SEQ.ID.NO:1333	-5.1	-20.1	64.5	-15	0	-2.7
238	ATCCAGGAAACTAAGAGAAG SEQ.ID.NO:1334	-5.1	-18.1	55.6	-12.4	-0.3	-5.7
393	GAAAATTCATCTGTGGTAGG SEQ.ID.NO:1335	-5.1	-19.5	59.9	-14.4	0	-4.1
595	TTCATATATTCCAGGAGAGT SEQ.ID.NO:1336	-5.1	-21.4	65.5	-16.3	0	-5.3
596	GTTCATATATTCCAGGAGAG SEQ.ID.NO:1337	-5.1	-21.4	65.5	-16.3	0	-5.3
831	CCGTTTTTACACTTGTACAC SEQ.ID.NO:1338	-5.1	-22.2	65.2	-16.4	-0.4	-6.6
950	TAGATTTACACTGAATTTCA SEQ.ID.NO:1339	-5.1	-17.4	55.5	-12.3	0	-5.7
1026	TGTCGCAAGTCACGACCTTC SEQ.ID.NO:1340	-5.1	-25.7	71.9	-17.8	-2.8	-7.8
1027	TTGTCGCAAGTCACGACCTT SEQ.ID.NO:1341	-5.1	-25.4	70.7	-17.5	-2.8	-7.8
1108	ATCCATAATAAAATGTAGAA SEQ.ID.NO:1342	-5.1	-14.5	48.1	-9.4	0	-2.8
1235	ATTCTACAAGAACCTGTACA SEQ.ID.NO:1343	-5.1	-20.1	60.5	-14	-0.9	-7.6
1323	AGGAACATAGCTTCAACCGC SEQ.ID.NO:1344	-5.1	-23.7	66.7	-18.1	-0.2	-4.6
1399	ACTATTTCGAATTCTTTCTT SEQ.ID.NO:1345	-5.1	-19.1	59.5	-13.2	-0.6	-6.4
1478	ACTCCTCTTGAGTCATTTTC SEQ.ID.NO:1346	-5.1	-23.4	71.7	-16.8	-1.4	-5.8

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intramolecular oligo	kcal/mol Intermolecular oligo
1490	TAAGCAGAGCATACTCCTCT SEQ.ID.NO:1347	-5.1	-24	70.4	-17.4	-1.4	-6.3
1570	AAGAAGTGGCTCCTGAAGCT SEQ.ID.NO:1348	-5.1	-24.2	69.4	-17	-2.1	-6.3
2000	TTAATTAGGCAAACAGGGCT SEQ.ID.NO:1349	-5.1	-21.2	62.3	-15.4	-0.5	-7.1
2069	GCAATATGGTAAGATGAGCA SEQ.ID.NO:1350	-5.1	-20.6	61.6	-15.5	0	-4.2
2111	CTTTATTGCCAAGATTGAAT SEQ.ID.NO:1351	-5.1	-19.3	58.3	-14.2	0	-3.7
109	CCTGGGAGGATTCTGGACTG SEQ.ID.NO:1352	-5	-26	73.9	-20.5	-0.1	-3.6
177	CTTTCACTCCTTCTACGATG SEQ.ID.NO:1353	-5	-23.3	68	-18.3	0	-3.5
563	GCTGCTGGGGGTAGAAACCC SEQ.ID.NO:1354	-5	-28.5	77.5	-20.5	-3	-11.2
582	GGAGAGTACCACTCTTCAGG SEQ.ID.NO:1355	-5	-25	73.9	-17.3	-2.7	-8.6
586	TCCAGGAGAGTACCACTCTT SEQ.ID.NO:1356	-5	-25.8	74.9	-18.1	-2.7	-8.3
655	AGGCATCTCTGCTACCTCAG SEQ.ID.NO:1357	-5	-26.9	78.2	-19.7	-2.2	-5.6
854	ACATATCCATCACACAGTTG SEQ.ID.NO:1358	-5	-21.9	65.1	-16.9	0	-2.6
866	TTCTTCGCATGTACATATCC SEQ.ID.NO:1359	-5	-23.1	67.9	-17.6	0	-8
1150	TTTATTTGTTATTTCCTGAG SEQ.ID.NO:1360	-5	-19.2	60.5	-14.2	0	-1.9
1161	TCTTTTAAAATTTTATTTGT SEQ.ID.NO:1361	-5	-14.6	49.6	-9.1	-0.2	-7.7
1266	AAAGTCTGAAATCCTGGTAG SEQ.ID.NO:1362	-5	-19.7	59.7	-14.7	0	-4.6
1640	GACCCAGGAGACAGGCAAAG SEQ.ID.NO:1363	-5	-25.1	69.5	-20.1	0	-4
1819	GGAAAGTTATACATCAGATT SEQ.ID.NO:1364	-5	-17.8	56.2	-12.8	0	-3.4
1866	ATATTCATCAAGATTTCTTG SEQ.ID.NO:1365	-5	-17.5	56.3	-11.4	-1	-8.5
2040	TTTCCCTAGTTCAACAGATA SEQ.ID.NO:1366	-5	-22.1	65.8	-17.1	0	-3.5
2096	TGAATACAACTCTTTAATAA SEQ.ID.NO:1367	-5	-14.4	48.4	-9.4	0	-2.5
88	GTCTTCCTCTCCAGATCCCA SEQ.ID.NO:1368	-4.9	-30	84.3	-25.1	0	-4.5
233	GGAAACTAAGAGAAGCAGTG SEQ.ID.NO:1369	-4.9	-18.7	57.2	-13.8	0	-4.1
300	GTGGTCTTCAAAAAAAACTC SEQ.ID.NO:1370	-4.9	-16.7	52.9	-11.8	0	-2.5
325	TCAATTGAAATGCACTTTCT SEQ.ID.NO:1371	-4.9	-18.8	57.6	-12.3	-1.6	-9.2
456	AGGTTCTGTCCCAGAGGACC SEQ.ID.NO:1372	-4.9	-28.7	81.6	-20.8	-3	-9.7
597	AGTTCATATATTCCAGGAGA SEQ.ID.NO:1373	-4.9	-21.4	65.5	-16.5	0	-5.3
625	GTAGAGAGTCTCAGCTGGCA	-4.9	-26.1	78.9	-19.8	-1.1	-10

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intra-molecular oligo	kcal/mol Inter-molecular oligo
	SEQ.ID.NO:1374						
1397	TATTTCGAATTCTTTCTTCC SEQ.ID.NO:1375	-4.9	-20.4	62.2	-14.7	-0.6	-6.7
1400	CACTATTTCGAATTCTTTCT SEQ.ID.NO:1376	-4.9	-19.7	60.4	-14	-0.6	-6.7
1487	GCAGAGCATACTCCTCTTGA SEQ.ID.NO:1377	-4.9	-25.7	74.8	-19.3	-1.4	-5.8
1695	CATGACATCAGCATCTCAGC SEQ.ID.NO:1378	-4.9	-24	70.9	-19.1	0	-4.1
1888	TACACATGTAATTACAACAT SEQ.ID.NO:1379	-4.9	-16.6	52.8	-10.5	-0.2	-10.3
1934	TAGAGAAAGTTGTTCTATCT SEQ.ID.NO:1380	-4.9	-18.4	59	-12	-1.4	-5.6
2067	AATATGGTAAGATGAGCAAA SEQ.ID.NO:1381	-4.9	-16.7	52.8	-11.8	0	-4.1
2073	ATATGCAATATGGTAAGATG SEQ.ID.NO:1382	-4.9	-17.2	54.3	-11.8	-0.2	-5.6
2084	TTTAATAAAATATATGCAAT SEQ.ID.NO:1383	-4.9	-12	43.4	-7.1	0	-5.6
2114	TTGCTTTATTGCCAAGATTG SEQ.ID.NO:1384	-4.9	-21.3	63.2	-16.4	0	-3.6
21	TCGGGGAGACAATGAGGTGA SEQ.ID.NO:1385	-4.8	-23.8	68	-19	0	-3.1
135	TTGGGTCAGAGATGGACTTT SEQ.ID.NO:1386	-4.8	-23.1	69.3	-17.1	-1.1	-5.3
271	TGAAGTTTCATCTTGAGGAA SEQ.ID.NO:1387	-4.8	-19.5	60.4	-14.7	0	-5.3
348	ATTTTTGATCCCATCCAAAT SEQ.ID.NO:1388	-4.8	-21.8	62.7	-16.3	-0.5	-4.3
377	TAGGTAAATGGGAATGTTCA SEQ.ID.NO:1389	-4.8	-19.1	58.6	-14.3	0	-5.7
954	CGCTTAGATTTACACTGAAT SEQ.ID.NO:1390	-4.8	-19.7	59.2	-14.9	0	-3.1
1092	AGAAGAGTCTGTTGATCTGG SEQ.ID.NO:1391	-4.8	-21.4	66.1	-16.1	-0.1	-5.8
1402	ACCACTATTTCGAATTCTTT SEQ.ID.NO:1392	-4.8	-20.6	61.4	-15.8	0	-6.7
195	TCTAAGTCTTCTTTTCTTCT SEQ.ID.NO:1393	-4.7	-21.2	67.6	-15.9	-0.3	-3
282	TCCAAAGTGTCTGAAGTTTC SEQ.ID.NO:1394	-4.7	-21.1	64.3	-16.4	0	-3
479	ATTGCGAGTATGGTTCCACT SEQ.ID.NO:1395	-4.7	-24.9	71.6	-20.2	0	-5.6
1077	TCTGGGGTGAGTTCAGTTTT SEQ.ID.NO:1396	-4.7	-24.6	75.3	-19.4	-0.2	-3.7
1604	GCTGGTGAATCTTACACAAC SEQ.ID.NO:1397	-4.7	-21.4	63.6	-15.1	-1.6	-5
1786	AAAAGGAGCTAGACCCCTCC SEQ.ID.NO:1398	-4.7	-26.2	71.1	-19.9	-1.6	-7.2
1838	TGGGTACAAGTGAAATAAAG SEQ.ID.NO:1399	-4.7	-16.2	51.7	-11.5	0	-5.2
2011	TAACAATCAATTTAATTAGG SEQ.ID.NO:1400	-4.7	-13.8	47.1	-9.1	0	-4.1
81	TCTCCAGATCCCAGCGATTT SEQ.ID.NO:1401	-4.6	-27.5	75.7	-22.9	0	-4.5

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intra-molecular oligo	kcal/mol Inter-molecular oligo
264	TCATCTTGAGGAAATGTCCA SEQ.ID.NO:1402	-4.6	-21.8	64.6	-15.1	-2.1	-5.7
521	AGGAAATCTGTGGTTGAACT SEQ.ID.NO:1403	-4.6	-20.4	61.6	-15.8	0	-3.4
1176	TCTGCACTGAATTCTTCTTT SEQ.ID.NO:1404	-4.6	-21.8	66.3	-16.5	-0.4	-6.9
1177	TTCTGCACTGAATTCTTCTT SEQ.ID.NO:1405	-4.6	-21.8	66.3	-16.5	-0.4	-6.9
1330	TGAACGAAGGAACATAGCTT SEQ.ID.NO:1406	-4.6	-19.3	57.4	-14.7	0	-4.6
1472	CTTGAGTCATTTTCAGTTCC SEQ.ID.NO:1407	-4.6	-23	70.6	-18.4	0	-5.8
1916	CTAGCCCAATATTTACAGTT SEQ.ID.NO:1408	-4.6	-22.2	65.1	-17.6	0	-4.1
2078	AAAATATATGCAATATGGTA SEQ.ID.NO:1409	-4.6	-14.9	49.1	-9.8	-0.2	-6.5
2086	TCTTTAATAAAATATATGCA SEQ.ID.NO:1410	-4.6	-14	47.6	-9.4	0	-5.2
241	GAAATCCAGGAAACTAAGAG SEQ.ID.NO:1411	-4.5	-17.4	53.7	-12.3	-0.3	-5.7
340	TCCCATCCAAATTTTTCAAT SEQ.ID.NO:1412	-4.5	-21.6	62.1	-17.1	0	-4.6
381	GTGGTAGGTAAATGGGAATG SEQ.ID.NO:1413	-4.5	-20.3	61.1	-15.8	0	-1.2
474	GAGTATGGTTCCACTTCCAG SEQ.ID.NO:1414	-4.5	-25.4	74.3	-20.4	-0.2	-5.1
868	CTTTCTTCGCATGTACATAT SEQ.ID.NO:1415	-4.5	-21.7	64.9	-16.7	0	-8
871	ACACTTTCTTCGCATGTACA SEQ.ID.NO:1416	-4.5	-23.1	67.9	-18.6	0	-6.4
1087	AGTCTGTTGATCTGGGGTGA SEQ.ID.NO:1417	-4.5	-25.1	75.7	-20.6	0	-4.9
1322	GGAACATAGCTTCAACCGCA SEQ.ID.NO:1418	-4.5	-24.4	67.6	-19.2	-0.5	-4.6
1527	ATGTATTGTCTATCTGGAGA SEQ.ID.NO:1419	-4.5	-20.9	65.2	-16.4	0	-3.3
1551	TTCTCTACTGCCTCTCTATC SEQ.ID.NO:1420	-4.5	-24.9	75.4	-20.4	0	-3
1750	CTGCACGTCCCAGATTTCAC SEQ.ID.NO:1421	-4.5	-26.8	74.4	-22.3	0	-6
2036	CCTAGTTCAACAGATAGAAT SEQ.ID.NO:1422	-4.5	-19.4	59.3	-14.9	0	-3.7
2083	TTAATAAAATATATGCAATA SEQ.ID.NO:1423	-4.5	-11.6	42.6	-7.1	0	-5.6
31	TTAGGATAAGTCGGGGAGAC SEQ.ID.NO:1424	-4.4	-22	65.2	-16.5	-1	-4.7
156	CTTCTACCTCCTTGGATTGT SEQ.ID.NO:1425	-4.4	-25.6	74.1	-20.5	-0.5	-4.6
480	TATTGCGAGTATGGTTCCAC SEQ.ID.NO:1426	-4.4	-23.7	69	-19.3	0	-5.6
1028	CTTGTCGCAAGTCACGACCT SEQ.ID.NO:1427	-4.4	-26.2	72.2	-19	-2.8	-8
1244	TTTTTGTGAATTCTACAAGA SEQ.ID.NO:1428	-4.4	-17.4	55.6	-11.6	-0.7	-10.5
1318	CATAGCTTCAACCGCAGACC	-4.4	-25.9	71	-20.8	-0.5	-4.6

position	oligo	kcal/ mol total binding	kcal/ mol duplex forma- tion	deg C Tm of Duplex	kcal/ mol target struc- ture	kcal/ mol Intra- mole- cular oligo	kcal/ mol Inter- mole- cular oligo
	SEQ.ID.NO:1429						
1359	GACGGAAGTTTCTTATTGAA SEQ.ID.NO:1430	-4.4	-19.2	58.6	-13.9	-0.8	-5.7
1744	GTCCCAGATTTCACAGAGAA SEQ.ID.NO:1431	-4.4	-23.6	68.7	-18.7	-0.1	-4.4
1820	AGGAAAGTTATACATCAGAT SEQ.ID.NO:1432	-4.4	-17.7	56.1	-13.3	0	-3.3
1867	AATATTCATCAAGATTTCTT SEQ.ID.NO:1433	-4.4	-16.8	54.4	-12.4	0	-4.7
2079	TAAAATATATGCAATATGGT SEQ.ID.NO:1434	-4.4	-14.9	49.1	-9.8	-0.5	-6.5
390	AATTCATCTGTGGTAGGTAA SEQ.ID.NO:1435	-4.3	-20.5	63.3	-16.2	0	-2.8
769	CTCACAGGTCAGTGCATTAT SEQ.ID.NO:1436	-4.3	-23.9	71.7	-18.9	-0.5	-5.4
818	TGTACACAGCGTTTTTGGTA SEQ.ID.NO:1437	-4.3	-23	68.2	-18.7	0	-5.9
861	CGCATGTACATATCCATCAC SEQ.ID.NO:1438	-4.3	-23.2	66.6	-18.4	0	-8
948	GATTTACACTGAATTTCAGT SEQ.ID.NO:1439	-4.3	-18.9	59.1	-12.3	-2.3	-11
1175	CTGCACTGAATTCTTCTTTT SEQ.ID.NO:1440	-4.3	-21.5	65.1	-16.5	-0.4	-6.9
1410	TCAGAGATACCACTATTTCG SEQ.ID.NO:1441	-4.3	-21.1	62.9	-16.1	-0.5	-3.6
1467	GTCATTTTCAGTTCCCCAAT SEQ.ID.NO:1442	-4.3	-25.4	72.9	-21.1	0	-1.5
1468	AGTCATTTTCAGTTCCCCAA SEQ.ID.NO:1443	-4.3	-25.4	73.2	-21.1	0	-0.9
1501	AACAATTGCTGTAAGCAGAG SEQ.ID.NO:1444	-4.3	-19.6	59.4	-12.2	-3.1	-9.1
1856	AGATTTCTTGAGTGAAACTG SEQ.ID.NO:1445	-4.3	-18.3	57.6	-12.8	-1.1	-5.5
1969	ATGCAGGATTCCCTGGAGCC SEQ.ID.NO:1446	-4.3	-29.3	80.2	-22	-3	-9.1
2037	CCCTAGTTCAACAGATAGAA SEQ.ID.NO:1447	-4.3	-21.4	63	-17.1	0	-3.7
2102	CAAGATTGAATACAACTCTT SEQ.ID.NO:1448	-4.3	-17	53.7	-10.8	-1.9	-5.4
25	TAAGTCGGGGAGACAATGAG SEQ.ID.NO:1449	-4.2	-21	61.9	-14.7	-2.1	-4.9
181	TCTTCTTTCACTCCTTCTAC SEQ.ID.NO:1450	-4.2	-23.7	72.5	-19.5	0	-0.2
368	GGGAATGTTCAATGAGATTC SEQ.ID.NO:1451	-4.2	-19.7	60.5	-15.5	0.2	-6.4
465	TCCACTTCCAGGTTCTGTCC SEQ.ID.NO:1452	-4.2	-28.8	82.7	-24.1	-0.2	-3.8
1411	ATCAGAGATACCACTATTTC SEQ.ID.NO:1453	-4.2	-20.3	62.4	-16.1	0	-3.3
1706	CGTTTACTCTCCATGACATC SEQ.ID.NO:1454	-4.2	-23.3	68.1	-19.1	0	-4.5
1999	TAATTAGGCAAACAGGGCTT SEQ.ID.NO:1455	-4.2	-21.2	62.3	-16.3	-0.5	-6.1
2033	AGTTCAACAGATAGAATTGA SEQ.ID.NO:1456	-4.2	-17.5	55.6	-12.6	-0.4	-4.2

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intramolecular oligo	kcal/mol Intermolecular oligo
2070	TGCAATATGGTAAGATGAGC SEQ.ID.NO:1457	-4.2	-19.9	60.3	-15.7	0	-4.7
134	TGGGTCAGAGATGGACTTTC SEQ.ID.NO:1458	-4.1	-23.4	70.6	-18.1	-1.1	-5
186	TCTTTTCTTCTTTCACTCCT SEQ.ID.NO:1459	-4.1	-24	73.3	-19.9	0	0
534	TAATAGGATGACGAGGAAAT SEQ.ID.NO:1460	-4.1	-17.1	53	-13	0	-3.5
535	ATAATAGGATGACGAGGAAA SEQ.ID.NO:1461	-4.1	-17.1	53	-13	0	-3.5
770	CCTCACAGGTCAGTGCATTA SEQ.ID.NO:1462	-4.1	-25.9	75.6	-21.1	-0.5	-5.4
771	CCCTCACAGGTCAGTGCATT SEQ.ID.NO:1463	-4.1	-28.2	79.9	-23.4	-0.5	-6.2
820	CTTGTACACAGCGTTTTTGG SEQ.ID.NO:1464	-4.1	-23.1	67.8	-19	0	-6.2
1316	TAGCTTCAACCGCAGACCCT SEQ.ID.NO:1465	-4.1	-28.1	75.1	-23.3	-0.5	-4.6
1629	CAGGCAAAGTGTTGAGGATT SEQ.ID.NO:1466	-4.1	-22	65.3	-17	-0.7	-4
1632	AGACAGGCAAAGTGTTGAGG SEQ.ID.NO:1467	-4.1	-22.1	65.7	-17.1	-0.7	-4
1711	GTGGTCGTTTACTCTCCATG SEQ.ID.NO:1468	-4.1	-25.4	74.4	-20.6	-0.4	-3.9
1752	CACTGCACGTCCCAGATTTC SEQ.ID.NO:1469	-4.1	-26.8	74.4	-22	-0.5	-7.5
2076	AATATATGCAATATGGTAAG SEQ.ID.NO:1470	-4.1	-15.6	50.8	-10.8	-0.5	-6.5
2097	TTGAATACAACTCTTTAATA SEQ.ID.NO:1471	-4.1	-15.2	50.3	-10.5	-0.3	-3.1
105	GGAGGATTCTGGACTGAGTC SEQ.ID.NO:1472	-4	-24.1	72.5	-19.6	-0.1	-5
355	GAGATTCATTTTTGATCCCA SEQ.ID.NO:1473	-4	-22.5	66.4	-17.6	-0.8	-4.5
429	TGTTCTGTTAAAACACCAAA SEQ.ID.NO:1474	-4	-17.9	54.9	-13.2	-0.5	-5.3
457	CAGGTTCTGTCCCAGAGGAC SEQ.ID.NO:1475	-4	-27.4	79	-20.8	-2.6	-8.3
754	ATTATAGTGGTATCCAGAGG SEQ.ID.NO:1476	-4	-21.7	66.2	-16.9	-0.6	-6.9
833	CCCCGTTTTTACACTTGTAC SEQ.ID.NO:1477	-4	-25.3	70.7	-20.6	-0.4	-4.5
867	TTTCTTCGCATGTACATATC SEQ.ID.NO:1478	-4	-21.2	64.5	-16.7	0	-8
926	ACAAGCATTCAGCCAACATT SEQ.ID.NO:1479	-4	-22.7	65.2	-17.7	-0.9	-4.1
1193	AAATGAGAAAATTTTCTTCT SEQ.ID.NO:1480	-4	-14.7	49.1	-8.8	-0.4	-11.9
1329	GAACGAAGGAACATAGCTTC SEQ.ID.NO:1481	-4	-19.7	58.7	-14.7	-0.9	-4.6
1502	TAACAATTGCTGTAAGCAGA SEQ.ID.NO:1482	-4	-19.3	58.6	-12.2	-3.1	-9.1
1561	CTCCTGAAGCTTCTCTACTG SEQ.ID.NO:1483	-4	-24.3	71.5	-19.2	0	-10.1
1730	AGAGAAGTGGGGTAAACTTG	-4	-20	60.7	-15	-0.9	-4.1

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intra-molecular oligo	kcal/mol Inter-molecular oligo
	SEQ.ID.NO:1484						
1768	CCCCTGTAATCCCCATCACT SEQ.ID.NO:1485	-4	-30.4	79	-26.4	0	-1.8
2023	ATAGAATTGAAGTAACAATC SEQ.ID.NO:1486	-4	-14.4	48.5	-9.7	-0.4	-3.9
184	TTTTCTTCTTTCACTCCTTC SEQ.ID.NO:1487	-3.9	-23.2	71.6	-19.3	0	0
388	TTCATCTGTGGTAGGTAAAT SEQ.ID.NO:1488	-3.9	-20.5	63.3	-16.6	0	-2.8
394	AGAAAATTCATCTGTGGTAG SEQ.ID.NO:1489	-3.9	-18.3	57.5	-14.4	0	-4.8
648	TCTGCTACCTCAGTTTCTCC SEQ.ID.NO:1490	-3.9	-27	79.6	-22.6	-0.2	-3.6
1747	CACGTCCCAGATTTCACAGA SEQ.ID.NO:1491	-3.9	-25.4	71.2	-21.5	0	-4.6
1771	CCTCCCCTGTAATCCCCATC SEQ.ID.NO:1492	-3.9	-31.9	82.3	-28	0	-1.6
1887	ACACATGTAATTACAACATA SEQ.ID.NO:1493	-3.9	-16.6	52.8	-11.6	-0.6	-9.8
2038	TCCCTAGTTCAACAGATAGA SEQ.ID.NO:1494	-3.9	-22.5	66.6	-18.6	0	-3.6
2055	TGAGCAAAATGAGATTTTCC SEQ.ID.NO:1495	-3.9	-18.9	57.5	-14.1	-0.7	-4.8
2071	ATGCAATATGGTAAGATGAG SEQ.ID.NO:1496	-3.9	-18.1	56.3	-14.2	0	-5.6
251	ATGTCCAGAAGAAATCCAGG SEQ.ID.NO:1497	-3.8	-21.7	63.1	-17.9	0	-3.3
267	GTTTCATCTTGAGGAAATGT SEQ.ID.NO:1498	-3.8	-20.1	62	-15.4	-0.7	-7.9
389	ATTCATCTGTGGTAGGTAAA SEQ.ID.NO:1499	-3.8	-20.5	63.3	-16.7	0	-2.8
391	AAATTCATCTGTGGTAGGTA SEQ.ID.NO:1500	-3.8	-20.5	63.3	-16.7	0	-3.1
519	GAAATCTGTGGTTGAACTTG SEQ.ID.NO:1501	-3.8	-19.3	59.1	-15.5	0	-3.4
594	TCATATATTCCAGGAGAGTA SEQ.ID.NO:1502	-3.8	-21	64.5	-17.2	0	-5.3
719	CAACACACAGCTCATCCCCT SEQ.ID.NO:1503	-3.8	-27.8	75.1	-24	0	-4.4
830	CGTTTTTACACTTGTACACA SEQ.ID.NO:1504	-3.8	-20.9	62.7	-16.4	-0.4	-6.6
855	TACATATCCATCACACAGTT SEQ.ID.NO:1505	-3.8	-21.6	64.7	-17.8	0	-2.6
949	AGATTTACACTGAATTTCAG SEQ.ID.NO:1506	-3.8	-17.7	56.3	-12.3	-1.6	-9.6
1201	TTCCGTCAAAATGAGAAAAT SEQ.ID.NO:1507	-3.8	-16.6	51.4	-12.8	0.4	-3.3
1504	GATAACAATTGCTGTAAGCA SEQ.ID.NO:1508	-3.8	-19.3	58.4	-12.6	-2.9	-7.7
1641	CGACCCAGGAGACAGGCAAA SEQ.ID.NO:1509	-3.8	-25.9	69.3	-22.1	0	-4
2054	GAGCAAAATGAGATTTTCCC SEQ.ID.NO:1510	-3.8	-20.9	61.2	-16.1	-0.9	-4.8
285	AACTCCAAAGTGTCTGAAGT SEQ.ID.NO:1511	-3.7	-20.9	62.5	-16.5	-0.5	-5

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intra-molecular oligo	kcal/mol Inter-molecular oligo
538	GGAATAATAGGATGACGAGG SEQ.ID.NO:1512	-3.7	-19	57.1	-15.3	0	-3.5
631	TCCCTGGTAGAGAGTCTCAG SEQ.ID.NO:1513	-3.7	-26.2	77.8	-21.1	-1.1	-10
746	GGTATCCAGAGGCTCTGTCT SEQ.ID.NO:1514	-3.7	-27.5	81.5	-22.2	-1.5	-8
790	CCTGAAGAAACCTTTACACC SEQ.ID.NO:1515	-3.7	-22.1	62.4	-18.4	0	-2.8
1333	AGCTGAACGAAGGAACATAG SEQ.ID.NO:1516	-3.7	-19.2	57.3	-15.5	0	-4.3
1635	AGGAGACAGGCAAAGTGTTG SEQ.ID.NO:1517	-3.7	-22.1	65.7	-17.8	-0.3	-4
1694	ATGACATCAGCATCTCAGCG SEQ.ID.NO:1518	-3.7	-24.1	69.8	-19.4	-0.9	-4.1
1751	ACTGCACGTCCCAGATTTCA SEQ.ID.NO:1519	-3.7	-26.8	74.4	-22.4	-0.5	-7.5
1828	TGAAATAAAGGAAAGTTATA SEQ.ID.NO:1520	-3.7	-12.6	44.6	-8.9	0	-2.8
2028	AACAGATAGAATTGAAGTAA SEQ.ID.NO:1521	-3.7	-14.6	48.8	-10.9	0	-3.1
76	AGATCCCAGCGATTTTGCTA SEQ.ID.NO:1522	-3.6	-25.6	71.8	-20.4	-1.6	-7.7
304	TATGGTGGTCTTCAAAAAAA SEQ.ID.NO:1523	-3.6	-16.8	52.9	-13.2	0	-3.3
326	TTCAATTGAAATGCACTTTC SEQ.ID.NO:1524	-3.6	-18	56.1	-13.2	-0.8	-9.9
797	TGCTTCTCCTGAAGAAACCT SEQ.ID.NO:1525	-3.6	-23.6	67.1	-17.8	-2.2	-5.7
821	ACTTGTACACAGCGTTTTTG SEQ.ID.NO:1526	-3.6	-22.1	65.8	-18.5	0	-6.3
1731	CAGAGAAGTGGGGTAAACTT SEQ.ID.NO:1527	-3.6	-20.7	62	-16.6	-0.1	-3.4
1861	CATCAAGATTTCTTGAGTGA SEQ.ID.NO:1528	-3.6	-19.7	61.1	-13.7	-2.4	-11.2
1915	TAGCCCAATATTTACAGTTG SEQ.ID.NO:1529	-3.6	-21.3	63.1	-17.7	0	-4.1
133	GGGTCAGAGATGGACTTTCA SEQ.ID.NO:1530	-3.5	-24.1	72	-19.4	-1.1	-5.3
138	GTTTTGGGTCAGAGATGGAC SEQ.ID.NO:1531	-3.5	-23.4	70.7	-19	-0.7	-4.7
242	AGAAATCCAGGAAACTAAGA SEQ.ID.NO:1532	-3.5	-17.4	53.7	-13.3	-0.3	-5.2
250	TGTCCAGAAGAAATCCAGGA SEQ.ID.NO:1533	-3.5	-22.3	64.4	-17.9	-0.7	-5.3
392	AAAATTCATCTGTGGTAGGT SEQ.ID.NO:1534	-3.5	-20.1	61.7	-16.6	0	-3.1
448	TCCCAGAGGACCTGCCACTT SEQ.ID.NO:1535	-3.5	-30.3	81.1	-25.7	-1	-6.7
782	AACCTTTACACCCCTCACAG SEQ.ID.NO:1536	-3.5	-26.3	71.6	-22.8	0	-1.2
1078	ATCTGGGGTGAGTTCAGTTT SEQ.ID.NO:1537	-3.5	-24.5	74.9	-20.5	-0.2	-3.7
1115	TATATGAATCCATAATAAAA SEQ.ID.NO:1538	-3.5	-13	45.1	-8.4	-1	-4.2
1204	CATTTCCGTCAAAATGAGAA	-3.5	-18.8	56.1	-14.1	-1.1	-5.2

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intramolecular oligo	kcal/mol Intermolecular oligo
	SEQ.ID.NO:1539						
1319	ACATAGCTTCAACCGCAGAC SEQ.ID.NO:1540	-3.5	-24.1	68.1	-20.6	0.3	-4.6
1550	TCTCTACTGCCTCTCTATCC SEQ.ID.NO:1541	-3.5	-26.8	78.9	-23.3	0	-3
1769	TCCCCTGTAATCCCCATCAC SEQ.ID.NO:1542	-3.5	-29.9	78.8	-26.4	0	-1.6
376	AGGTAAATGGGAATGTTCAA SEQ.ID.NO:1543	-3.4	-18.7	57.3	-15.3	0	-5.7
1073	GGGTGAGTTCAGTTTTCTCC SEQ.ID.NO:1544	-3.4	-25.8	78.6	-21.8	-0.3	-3.6
1353	AGTTTCTTATTGAAAATCTC SEQ.ID.NO:1545	-3.4	-16.8	54.8	-11.9	-1.4	-4.5
1488	AGCAGAGCATACTCCTCTTG SEQ.ID.NO:1546	-3.4	-25.1	73.7	-20.2	-1.4	-6.3
1862	TCATCAAGATTTCTTGAGTG SEQ.ID.NO:1547	-3.4	-19.5	61.2	-13.7	-2.4	-11.2
1883	ATGTAATTACAACATAAATA SEQ.ID.NO:1548	-3.4	-13.1	45.6	-8.5	-0.4	-10.3
2029	CAACAGATAGAATTGAAGTA SEQ.ID.NO:1549	-3.4	-16	51.7	-12.6	0	-3.1
2035	CTAGTTCAACAGATAGAATT SEQ.ID.NO:1550	-3.4	-17.5	55.8	-14.1	0	-3.7
2052	GCAAAATGAGATTTTCCCTA SEQ.ID.NO:1551	-3.4	-20.9	61	-16.5	-0.9	-4.3
209	CTTTGAGCTATGTTTCTAAG SEQ.ID.NO:1552	-3.3	-19.8	61.9	-16.5	0	-4.5
1630	ACAGGCAAAGTGTTGAGGAT SEQ.ID.NO:1553	-3.3	-22.1	65.5	-18.8	0	-4
1917	TCTAGCCCAATATTTACAGT SEQ.ID.NO:1554	-3.3	-22.5	66.2	-19.2	0	-4.1
1919	TATCTAGCCCAATATTTACA SEQ.ID.NO:1555	-3.3	-21	62.3	-17.7	0	-4.1
182	TTCTTCTTTCACTCCTTCTA SEQ.ID.NO:1556	-3.2	-23.6	72.3	-20.4	0	0
395	AAGAAAATTCATCTGTGGTA SEQ.ID.NO:1557	-3.2	-17.6	55.4	-14.4	0	-4.8
428	GTTCTGTTAAAACACCAAAT SEQ.ID.NO:1558	-3.2	-17.9	54.9	-14.7	0	-5.5
621	AGAGTCTCAGCTGGCATACG SEQ.ID.NO:1559	-3.2	-25.3	73.6	-21.5	0	-8.6
629	CCTGGTAGAGAGTCTCAGCT SEQ.ID.NO:1560	-3.2	-26.5	78.9	-21.9	-1.1	-10
858	ATGTACATATCCATCACACA SEQ.ID.NO:1561	-3.2	-21.5	64	-17.8	0	-7.6
1178	CTTCTGCACTGAATTCTTCT SEQ.ID.NO:1562	-3.2	-22.6	67.9	-18.7	-0.4	-6.9
1286	CAATCTGGTCTTCATGGTCC SEQ.ID.NO:1563	-3.2	-25	73.6	-21.8	0	-4.7
1437	AAACTAAACATAGGTGTTAT SEQ.ID.NO:1564	-3.2	-16	51.7	-11.1	-1.7	-5.8
1732	ACAGAGAAGTGGGGTAAACT SEQ.ID.NO:1565	-3.2	-20.8	62.2	-17.6	0	-2.9
1918	ATCTAGCCCAATATTTACAG SEQ.ID.NO:1566	-3.2	-21.3	63	-18.1	0	-4.1

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intra-molecular oligo	kcal/mol Inter-molecular oligo
2080	ATAAAATATATGCAATATGG SEQ.ID.NO:1567	-3.2	-13.7	46.6	-9.8	-0.5	-6
279	AAAGTGTCTGAAGTTTCATC SEQ.ID.NO:1568	-3.1	-19.1	60.3	-16	0	-4.7
731	TGTCTCCACAAACAACACAC SEQ.ID.NO:1569	-3.1	-21.3	61.9	-18.2	0	-2.8
1174	TGCACTGAATTCTTCTTTTA SEQ.ID.NO:1570	-3.1	-20.3	62.5	-16.5	-0.4	-6.9
1741	CCAGATTTCACAGAGAAGTG SEQ.ID.NO:1571	-3.1	-21.2	63.6	-17.5	-0.3	-4.5
1743	TCCCAGATTTCACAGAGAAG SEQ.ID.NO:1572	-3.1	-22.4	65.7	-18.7	-0.3	-3.7
1774	ACCCCTCCCCTGTAATCCCC SEQ.ID.NO:1573	-3.1	-35	86.5	-31.9	0	-1.7
26	ATAAGTCGGGGAGACAATGA SEQ.ID.NO:1574	-3	-21	61.7	-15.9	-2.1	-5.1
179	TTCTTTCACTCCTTCTACGA SEQ.ID.NO:1575	-3	-23.8	70.1	-20.8	0	-3.5
235	CAGGAAACTAAGAGAAGCAG SEQ.ID.NO:1576	-3	-18.2	55.9	-14.6	-0.3	-4.7
334	CCAAATTTTTCAATTGAAAT SEQ.ID.NO:1577	-3	-15.4	49.6	-10.3	-0.5	-12.4
387	TCATCTGTGGTAGGTAAATG SEQ.ID.NO:1578	-3	-20.4	62.8	-17.4	0	-2.8
458	CCAGGTTCTGTCCCAGAGGA SEQ.ID.NO:1579	-3	-29.2	82	-24.8	-1.3	-6.8
460	TTCCAGGTTCTGTCCCAGAG SEQ.ID.NO:1580	-3	-27.9	80.2	-23.6	-1.2	-7
497	GAAACTGAACATTGCTGTAT SEQ.ID.NO:1581	-3	-18.8	57.3	-15.1	-0.5	-3.9
768	TCACAGGTCAGTGCATTATA SEQ.ID.NO:1582	-3	-22.7	69	-19	-0.5	-5.4
956	GTCGCTTAGATTTACACTGA SEQ.ID.NO:1583	-3	-22	65.7	-19	0	-3.1
1197	GTCAAAATGAGAAAATTTTC SEQ.ID.NO:1584	-3	-14	47.5	-9.8	-0.7	-10.1
1205	CCATTTCCGTCAAAATGAGA SEQ.ID.NO:1585	-3	-21.5	61.4	-16.9	-1.6	-6
1403	TACCACTATTTCGAATTCTT SEQ.ID.NO:1586	-3	-20.2	60.5	-17.2	0	-6.7
1508	ACAGGATAACAATTGCTGTA SEQ.ID.NO:1587	-3	-19.6	59.4	-15.6	-0.9	-7.7
161	GATGTCTTCTACCTCCTTGG SEQ.ID.NO:1588	-2.9	-25.9	75.5	-22.5	-0.1	-3.2
178	TCTTTCACTCCTTCTACGAT SEQ.ID.NO:1589	-2.9	-23.7	69.7	-20.8	0	-3.5
632	CTCCCTGGTAGAGAGTCTCA SEQ.ID.NO:1590	-2.9	-27.1	79.5	-22.8	-1.1	-10
1103	TAATAAAATGTAGAAGAGTC SEQ.ID.NO:1591	-2.9	-13.6	47	-10.7	0	-3.5
1705	GTTTACTCTCCATGACATCA SEQ.ID.NO:1592	-2.9	-23.2	69.2	-20.3	0	-4.5
1870	ATAAATATTCATCAAGATTT SEQ.ID.NO:1593	-2.9	-14.4	48.7	-11.5	4	-4.6
249	GTCCAGAAGAAATCCAGGAA	-2.8	-21.6	62.5	-17.8	-0.9	-5.7

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intra-molecular oligo	kcal/mol Inter-molecular oligo
	SEQ.ID.NO:1594						
396	AAAGAAAATTCATCTGTGGT SEQ.ID.NO:1595	-2.8	-17.2	54.2	-14.4	0	-4.8
628	CTGGTAGAGAGTCTCAGCTG SEQ.ID.NO:1596	-2.8	-24.5	74.7	-20.3	-1.1	-10
1194	AAAATGAGAAAATTTTCTTC SEQ.ID.NO:1597	-2.8	-13.1	45.8	-8.1	-1	-12.5
1466	TCATTTTCAGTTCCCCAATA SEQ.ID.NO:1598	-2.8	-23.9	69	-21.1	0	-1.7
1708	GTCGTTTACTCTCCATGACA SEQ.ID.NO:1599	-2.8	-24.5	71.5	-21.1	-0.3	-4.6
20	CGGGGAGACAATGAGGTGAG SEQ.ID.NO:1600	-2.7	-23.4	66.8	-20.7	0	-3.1
30	TAGGATAAGTCGGGGAGACA SEQ.ID.NO:1601	-2.7	-22.6	66.1	-17.8	-2.1	-4.9
59	CTACAAATGCTCAGAATCCA SEQ.ID.NO:1602	-2.7	-20.9	61.2	-18.2	0	-3.6
187	TTCTTTTCTTCTTTCACTCC SEQ.ID.NO:1603	-2.7	-23.2	71.6	-20.5	0	0
383	CTGTGGTAGGTAAATGGGAA SEQ.ID.NO:1604	-2.7	-21.2	63.1	-18.5	0	-1.2
452	TCTGTCCCAGAGGACCTGCC SEQ.ID.NO:1605	-2.7	-30.9	84.3	-25.2	-3	-8.6
475	CGAGTATGGTTCCACTTCCA SEQ.ID.NO:1606	-2.7	-26.2	73.8	-22.8	-0.5	-5.6
522	GAGGAAATCTGTGGTTGAAC SEQ.ID.NO:1607	-2.7	-20.1	60.9	-17.4	0	-3
779	CTTTACACCCCTCACAGGTC SEQ.ID.NO:1608	-2.7	-27.6	77.3	-24.2	-0.5	-4.1
937	AATTTCAGTTAACAAGCATT SEQ.ID.NO:1609	-2.7	-17.7	55.7	-15	0	-7.3
1021	CAAGTCACGACCTTCACTGT SEQ.ID.NO:1610	-2.7	-24.5	69.8	-21.8	0	-4.7
1321	GAACATAGCTTCAACCGCAG SEQ.ID.NO:1611	-2.7	-23.2	65.4	-19.8	-0.5	-4.6
1339	AATCTCAGCTGAACGAAGGA SEQ.ID.NO:1612	-2.7	-21	61.4	-17.2	0	-10.1
1484	GAGCATACTCCTCTTGAGTC SEQ.ID.NO:1613	-2.7	-24.8	74.5	-20.4	-1.7	-7.5
1507	CAGGATAACAATTGCTGTAA SEQ.ID.NO:1614	-2.7	-18.7	57	-15.3	-0.4	-7
1699	TCTCCATGACATCAGCATCT SEQ.ID.NO:1615	-2.7	-24.8	72.5	-22.1	0	-4.5
1998	AATTAGGCAAACAGGGCTTG SEQ.ID.NO:1616	-2.7	-21.5	62.8	-18.1	-0.5	-4
449	GTCCCAGAGGACCTGCCACT SEQ.ID.NO:1617	-2.6	-31.4	84.3	-26.5	-2.3	-7.6
714	CACAGCTCATCCCCTTTGAT SEQ.ID.NO:1618	-2.6	-27.5	76.1	-24.9	0	-4.4
927	AACAAGCATTCAGCCAACAT SEQ.ID.NO:1619	-2.6	-21.9	62.8	-18.8	-0.1	-3.9
958	CAGTCGCTTAGATTTACACT SEQ.ID.NO:1620	-2.6	-22.1	66	-19.5	0	-3.1
1192	AATGAGAAAATTTTCTTCTG SEQ.ID.NO:1621	-2.6	-15.4	50.7	-10.6	-1	-12.5

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intramolecular oligo	kcal/mol Intermolecular oligo
1412	CATCAGAGATACCACTATTT SEQ.ID.NO:1622	-2.6	-20.6	62.2	-18	0	-3.5
1465	CATTTTCAGTTCCCCAATAC SEQ.ID.NO:1623	-2.6	-23.7	68	-21.1	0	-2
1770	CTCCCCTGTAATCCCCATCA SEQ.ID.NO:1624	-2.6	-30.6	80.1	-28	0	-1.7
2032	GTTCAACAGATAGAATTGAA SEQ.ID.NO:1625	-2.6	-16.8	53.6	-12.6	-1.6	-5.7
29	AGGATAAGTCGGGGAGACAA SEQ.ID.NO:1626	-2.5	-22.2	64.5	-17.6	-2.1	-4.9
248	TCCAGAAGAAATCCAGGAAA SEQ.ID.NO:1627	-2.5	-19.7	57.8	-16.5	-0.4	-5.7
332	AAATTTTTCAATTGAAATGC SEQ.ID.NO:1628	-2.5	-14.5	48.3	-10	-0.5	-12.1
374	GTAAATGGGAATGTTCAATG SEQ.ID.NO:1629	-2.5	-17.5	54.6	-15	0	-5.7
539	TGGAATAATAGGATGACGAG SEQ.ID.NO:1630	-2.5	-17.8	54.7	-15.3	0	-3.5
591	TATATTCCAGGAGAGTACCA SEQ.ID.NO:1631	-2.5	-22.8	67.4	-19.6	-0.5	-5
624	TAGAGAGTCTCAGCTGGCAT SEQ.ID.NO:1632	-2.5	-24.9	74.9	-21	-1.1	-10
788	TGAAGAAACCTTTACACCCC SEQ.ID.NO:1633	-2.5	-23.2	64	-20.7	0	-2.8
953	GCTTAGATTTACACTGAATT SEQ.ID.NO:1634	-2.5	-19	58.9	-16.5	0	-3.6
1083	TGTTGATCTGGGGTGAGTTC SEQ.ID.NO:1635	-2.5	-24.3	74	-21.8	0	-4.9
1241	TTGTGAATTCTACAAGAACC SEQ.ID.NO:1636	-2.5	-18.6	57.1	-14.9	-0.9	-9.9
1421	TTATATATTCATCAGAGATA SEQ.ID.NO:1637	-2.5	-16.4	54.1	-13.9	0	-3.9
1505	GGATAACAATTGCTGTAAGC SEQ.ID.NO:1638	-2.5	-19.8	59.7	-15.5	-1.8	-7.1
1628	AGGCAAAGTGTTGAGGATTT SEQ.ID.NO:1639	-2.5	-21.4	64.4	-18	-0.7	-4
331	AATTTTTCAATTGAAATGCA SEQ.ID.NO:1640	-2.4	-15.9	51.1	-11.4	-0.4	-12.4
375	GGTAAATGGGAATGTTCAAT SEQ.ID.NO:1641	-2.4	-18.7	57.1	-16.3	0	-5.7
427	TTCTGTTAAAACACCAAATA SEQ.ID.NO:1642	-2.4	-16.4	51.8	-14	0	-5.5
459	TCCAGGTTCTGTCCCAGAGG SEQ.ID.NO:1643	-2.4	-29	82.5	-25.3	-1.2	-7
716	CACACAGCTCATCCCCTTTG SEQ.ID.NO:1644	-2.4	-27.8	76.4	-25.4	0	-4.2
934	TTCAGTTAACAAGCATTCAG SEQ.ID.NO:1645	-2.4	-19.4	60.1	-17	0	-7.3
1203	ATTTCCGTCAAAATGAGAAA SEQ.ID.NO:1646	-2.4	-17.4	53.3	-14	-0.9	-5.1
1328	AACGAAGGAACATAGCTTCA SEQ.ID.NO:1647	-2.4	-19.8	58.6	-15.4	-2	-5.6
1463	TTTTCAGTTCCCCAATACTT SEQ.ID.NO:1648	-2.4	-24	69.2	-21.6	0	-2.7
2082	TAATAAAATATATGCAATAT	-2.4	-11.5	42.4	-8.5	-0.3	-6.2

position	oligo	kcal/ mol total binding	kcal/ mol duplex formation	deg C Tm of Duplex	kcal/ mol target structure	kcal/ mol Intra-molecular oligo	kcal/ mol Inter-molecular oligo
	SEQ.ID.NO:1649						
2085	CTTTAATAAAATATATGCAA SEQ.ID.NO:1650	-2.4	-12.9	45.1	-10.5	0	-5.6
18	GGGAGACAATGAGGTGAGGA SEQ.ID.NO:1651	-2.3	-23.2	67.9	-20.9	0	-3.1
384	TCTGTGGTAGGTAAATGGGA SEQ.ID.NO:1652	-2.3	-22.3	66.8	-20	0	-1.9
832	CCCGTTTTTACACTTGTACA SEQ.ID.NO:1653	-2.3	-24	68.3	-21	-0.4	-6.4
929	TTAACAAGCATTCAGCCAAC SEQ.ID.NO:1654	-2.3	-21	61.5	-17.7	-0.9	-4.1
1076	CTGGGGTGAGTTCAGTTTTC SEQ.ID.NO:1655	-2.3	-24.6	75.3	-22.3	0	-3.4
1162	TTCTTTTAAAATTTTATTTG SEQ.ID.NO:1656	-2.3	-13.5	47.2	-10.6	-0.2	-8
1471	TTGAGTCATTTTCAGTTCCC SEQ.ID.NO:1657	-2.3	-24.1	72.4	-21.8	0	-5.8
1625	CAAAGTGTTGAGGATTTTCA SEQ.ID.NO:1658	-2.3	-19.6	60.4	-17.3	0	-3
1868	AAATATTCATCAAGATTTCT SEQ.ID.NO:1659	-2.3	-16	52.3	-13.7	4.1	-4.6
382	TGTGGTAGGTAAATGGGAAT SEQ.ID.NO:1660	-2.2	-20.3	61.1	-18.1	0	-1.2
451	CTGTCCCAGAGGACCTGCCA SEQ.ID.NO:1661	-2.2	-31.2	83.4	-26	-3	-8.6
585	CCAGGAGAGTACCACTCTTC SEQ.ID.NO:1662	-2.2	-25.8	74.9	-21.3	-2.3	-7.5
772	CCCCTCACAGGTCAGTGCAT SEQ.ID.NO:1663	-2.2	-30.1	83	-27.2	-0.5	-6.2
817	GTACACAGCGTTTTTGGTAA SEQ.ID.NO:1664	-2.2	-22.3	66	-20.1	0	-4.6
1166	ATTCTTCTTTTAAAATTTTA SEQ.ID.NO:1665	-2.2	-14.7	49.9	-12	0	-7.7
1320	AACATAGCTTCAACCGCAGA SEQ.ID.NO:1666	-2.2	-23.2	65.4	-20.3	-0.5	-4.3
1664	TGAATGTCCGTAATTCAGTC SEQ.ID.NO:1667	-2.2	-21.3	63.7	-17.6	-1.4	-5.9
1855	GATTTCTTGAGTGAAACTGG SEQ.ID.NO:1668	-2.2	-19.5	60	-16.1	-1.1	-5.5
185	CTTTTCTTCTTTCACTCCTT SEQ.ID.NO:1669	-2.1	-23.7	71.9	-21.6	0	0
335	TCCAAATTTTTCAATTGAAA SEQ.ID.NO:1670	-2.1	-15.8	50.6	-11.7	-0.5	-12.1
352	ATTCATTTTTGATCCCATCC SEQ.ID.NO:1671	-2.1	-23.7	68.7	-20.7	-0.8	-4.3
354	AGATTCATTTTTGATCCCAT SEQ.ID.NO:1672	-2.1	-21.9	65	-18.9	-0.8	-4.5
545	CCAGGTTGGAATAATAGGAT SEQ.ID.NO:1673	-2.1	-20.8	61.5	-18.1	-0.3	-3.5
787	GAAGAAACCTTTACACCCCT SEQ.ID.NO:1674	-2.1	-24.1	65.8	-22	0	-2.8
856	GTACATATCCATCACACAGT SEQ.ID.NO:1675	-2.1	-22.7	67.6	-20.6	0	-4.6
1082	GTTGATCTGGGGTGAGTTCA SEQ.ID.NO:1676	-2.1	-25	75.4	-22.9	0	-4.9

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intra-molecular oligo	kcal/mol Inter-molecular oligo
1088	GAGTCTGTTGATCTGGGGTG SEQ.ID.NO:1677	-2.1	-25.1	75.7	-23	0	-4.9
1522	TTGTCTATCTGGAGACAGGA SEQ.ID.NO:1678	-2.1	-22.7	68.9	-18.2	-2.4	-8.9
1746	ACGTCCCAGATTTCACAGAG SEQ.ID.NO:1679	-2.1	-24.7	70.3	-22.6	0	-4.4
1882	TGTAATTACAACATAAATAT SEQ.ID.NO:1680	-2.1	-13.1	45.6	-10.2	0	-9.4
270	GAAGTTTCATCTTGAGGAAA SEQ.ID.NO:1681	-2	-18.8	58.4	-16.1	-0.5	-7.7
1102	AATAAAATGTAGAAGAGTCT SEQ.ID.NO:1682	-2	-14.8	49.5	-12.8	0	-5.5
1107	TCCATAATAAAATGTAGAAG SEQ.ID.NO:1683	-2	-14.5	48.2	-12.5	0	-2.8
1243	TTTTGTGAATTCTACAAGAA SEQ.ID.NO:1684	-2	-16.6	53.4	-13.2	-0.7	-10.5
1438	AAAACTAAACATAGGTGTTA SEQ.ID.NO:1685	-2	-15.3	50.1	-11.6	-1.7	-5.8
1493	CTGTAAGCAGAGCATACTCC SEQ.ID.NO:1686	-2	-23.9	70	-20.4	-1.4	-7.9
1511	GAGACAGGATAACAATTGCT SEQ.ID.NO:1687	-2	-19.9	59.8	-17.9	0	-7
1521	TGTCTATCTGGAGACAGGAT SEQ.ID.NO:1688	-2	-22.6	68.5	-18.2	-2.4	-8.6
2077	AAATATATGCAATATGGTAA SEQ.ID.NO:1689	-2	-14.9	49.1	-12.2	-0.5	-6.5
196	TTCTAAGTCTTCTTTTCTTC SEQ.ID.NO:1690	-1.9	-20.4	65.8	-17.9	-0.3	-3
373	TAAATGGGAATGTTCAATGA SEQ.ID.NO:1691	-1.9	-16.9	53.1	-15	0	-5.7
386	CATCTGTGGTAGGTAAATGG SEQ.ID.NO:1692	-1.9	-21.2	64	-19.3	0	-2.5
750	TAGTGGTATCCAGAGGCTCT SEQ.ID.NO:1693	-1.9	-25.9	77.1	-23.2	-0.6	-4.8
957	AGTCGCTTAGATTTACACTG SEQ.ID.NO:1694	-1.9	-21.4	64.6	-19.5	0	-3.1
1498	AATTGCTGTAAGCAGAGCAT SEQ.ID.NO:1695	-1.9	-21.9	65	-16.9	-3.1	-10.7
1767	CCCTGTAATCCCCATCACTG SEQ.ID.NO:1696	-1.9	-28.4	75.6	-26.5	0	-2.3
58	TACAAATGCTCAGAATCCAA SEQ.ID.NO:1697	-1.8	-19.3	57.6	-17.5	0	-3.6
755	CATTATAGTGGTATCCAGAG SEQ.ID.NO:1698	-1.8	-21.2	64.8	-18.6	-0.6	-6.9
800	TAATGCTTCTCCTGAAGAAA SEQ.ID.NO:1699	-1.8	-19.5	58.6	-16.1	-1.5	-6.7
1196	TCAAAATGAGAAAATTTTCT SEQ.ID.NO:1700	-1.8	-13.7	46.7	-9.8	-0.8	-12.3
1202	TTTCCGTCAAAATGAGAAAA SEQ.ID.NO:1701	-1.8	-16.7	51.7	-14.1	-0.6	-4.5
1358	ACGGAAGTTTCTTATTGAAA SEQ.ID.NO:1702	-1.8	-17.9	55.5	-14.8	-1.2	-6.6
1742	CCCAGATTTCACAGAGAAGT SEQ.ID.NO:1703	-1.8	-23.2	67.4	-20.8	-0.3	-3.7
1886	CACATGTAATTACAACATAA	-1.8	-15.7	50.6	-12.6	-0.6	-10.3

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intramolecular oligo	kcal/mol Intermolecular oligo
	SEQ.ID.NO:1704 ATTTAATTAGGCAAACAGGG						
2002	SEQ.ID.NO:1705 CCAGCGATTTTGCTACAAAT	-1.8	-18.6	56.9	-16.8	0	-4.1
71	SEQ.ID.NO:1706 CTGGGAGGATTCTGGACTGA	-1.7	-22.1	62.8	-18.8	-1.6	-7.2
108	SEQ.ID.NO:1707 CCCATCCAAATTTTTCAATT	-1.7	-24.6	71.6	-22.9	0	-2.7
339	SEQ.ID.NO:1708 TGGGAATGTTCAATGAGATT	-1.7	-21.3	61.1	-19	-0.3	-4.6
369	SEQ.ID.NO:1709 AGGAGAGTACCACTCTTCAG	-1.7	-19.3	59	-17.6	0	-5.7
583	SEQ.ID.NO:1710 ATATATTCCAGGAGAGTACC	-1.7	-23.8	71.4	-18.7	-3.4	-8.6
592	SEQ.ID.NO:1711 ACACACAGCTCATCCCCTTT	-1.7	-22.1	66.2	-20.4	0	-5.3
717	SEQ.ID.NO:1712 GTCTCCACAAACAACACACA	-1.7	-28	77.2	-26.3	0	-4.4
730	SEQ.ID.NO:1713 AATGCTTCTCCTGAAGAAAC	-1.7	-22	63.2	-20.3	0	-2.2
799	SEQ.ID.NO:1714 TACACAGCGTTTTTGGTAAT	-1.7	-20	59.7	-16.1	-2.2	-6.7
816	SEQ.ID.NO:1715 CTTCTTTTAAAATTTTATTT	-1.7	-21.1	62.9	-19.4	0	-4.1
1163	SEQ.ID.NO:1716 AAAGTGTTGAGGATTTTCAG	-1.7	-14.4	49.1	-12.2	0	-8
1624	SEQ.ID.NO:1717 GACCCCTCCCCTGTAATCCC	-1.7	-18.9	59.3	-17.2	0	-3.2
1775	SEQ.ID.NO:1718 ATTTACAGTTGTGGAAGTTA	-1.7	-33.6	84.7	-31.9	0	-2
1906	SEQ.ID.NO:1719 CAATATGGTAAGATGAGCAA	-1.7	-19.4	61	-17.7	0	-3.4
2068	SEQ.ID.NO:1720 AGTTTCATCTTGAGGAAATG	-1.7	-18.1	55.8	-16.4	0	-4.1
268	SEQ.ID.NO:1721 GATTCATTTTTGATCCCATC	-1.6	-18.9	59.1	-16.4	-0.7	-7.9
353	SEQ.ID.NO:1722 AATAATAGGATGACGAGGAA	-1.6	-22.3	66.3	-19.8	-0.8	-4.3
536	SEQ.ID.NO:1723 CCCAGGTTGGAATAATAGGA	-1.6	-17.1	53	-15.5	0	-3.5
546	SEQ.ID.NO:1724 ACACAGCGTTTTTGGTAATG	-1.6	-22.8	65.1	-20.3	-0.8	-4.3
815	SEQ.ID.NO:1725 TCGTTTACTCTCCATGACAT	-1.6	-21.4	63.3	-19.8	0	-3.7
1707	SEQ.ID.NO:1726 ATAAAGGAAAGTTATACATC	-1.6	-23.3	68.1	-21.7	0	-4.5
1824	SEQ.ID.NO:1727 TTCAACAGATAGAATTGAAG	-1.6	-14.7	49.2	-13.1	0	-2.7
2031	SEQ.ID.NO:1728 CTTGGATTGTTTTGGGTCAG	-1.6	-15.6	51	-12.6	-1.3	-5.1
146	SEQ.ID.NO:1729 CAAATTTTTCAATTGAAATG	-1.5	-23.1	69.7	-21.6	0	-3.4
333	SEQ.ID.NO:1730 CGAGGAAATCTGTGGTTGAA	-1.5	-13.4	46	-9.8	-0.5	-12.4
523	SEQ.ID.NO:1731	-1.5	-20.7	60.9	-19.2	0	-2.6

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intramolecular oligo	kcal/mol Intermolecular oligo
747	TGGTATCCAGAGGCTCTGTC SEQ.ID.NO:1732	-1.5	-26.6	79.1	-23.5	-1.5	-8
1340	AAATCTCAGCTGAACGAAGG SEQ.ID.NO:1733	-1.5	-19.7	58.3	-17.2	0	-9.9
1413	TCATCAGAGATACCACTATT SEQ.ID.NO:1734	-1.5	-20.9	63.3	-19.4	0	-3.5
1523	ATTGTCTATCTGGAGACAGG SEQ.ID.NO:1735	-1.5	-22.1	67.5	-18.2	-2.4	-8.2
72	CCCAGCGATTTTGCTACAAA SEQ.ID.NO:1736	-1.4	-24.1	66.2	-21.1	-1.6	-7.1
106	GGGAGGATTCTGGACTGAGT SEQ.ID.NO:1737	-1.4	-24.9	73.5	-23.5	0	-3.1
254	GAAATGTCCAGAAGAAATCC SEQ.ID.NO:1738	-1.4	-19	56.8	-17.6	0	-2.2
1324	AAGGAACATAGCTTCAACCG SEQ.ID.NO:1739	-1.4	-21.2	60.9	-19.3	-0.2	-4.6
1470	TGAGTCATTTTCAGTTCCCC SEQ.ID.NO:1740	-1.4	-26	75.9	-24.6	0	-5.4
1491	GTAAGCAGAGCATACTCCTC SEQ.ID.NO:1741	-1.4	-24.3	71.9	-21.4	-1.4	-6.3
1627	GGCAAAGTGTTGAGGATTTT SEQ.ID.NO:1742	-1.4	-21.5	64.5	-19.2	-0.7	-4
1878	ATTACAACATAAATATTCAT SEQ.ID.NO:1743	-1.4	-14.1	47.7	-12.7	0	-4.6
70	CAGCGATTTTGCTACAAATG SEQ.ID.NO:1744	-1.3	-20.1	59.2	-17.2	-1.6	-7.2
155	TTCTACCTCCTTGGATTGTT SEQ.ID.NO:1745	-1.3	-24.8	72.5	-23.5	0.2	-4.6
180	CTTCTTTCACTCCTTCTACG SEQ.ID.NO:1746	-1.3	-24.1	70.7	-22.8	0	-3
524	ACGAGGAAATCTGTGGTTGA SEQ.ID.NO:1747	-1.3	-21.6	63.4	-20.3	0	-3.5
525	GACGAGGAAATCTGTGGTTG SEQ.ID.NO:1748	-1.3	-21.6	63.4	-20.3	0	-3.5
562	CTGCTGGGGGTAGAAACCCA SEQ.ID.NO:1749	-1.3	-27.4	74.4	-22	-4.1	-10.8
1404	ATACCACTATTTCGAATTCT SEQ.ID.NO:1750	-1.3	-20.1	60.2	-18.8	0	-6.7
1464	ATTTTCAGTTCCCCAATACT SEQ.ID.NO:1751	-1.3	-23.9	68.8	-22.6	0	-2.8
1526	TGTATTGTCTATCTGGAGAC SEQ.ID.NO:1752	-1.3	-21.1	65.9	-18.7	-1	-4.8
1560	TCCTGAAGCTTCTCTACTGC SEQ.ID.NO:1753	-1.3	-25.2	73.9	-22.5	0	-10.8
1920	CTATCTAGCCCAATATTTAC SEQ.ID.NO:1754	-1.3	-21.2	63	-19.9	0	-4.1
2034	TAGTTCAACAGATAGAATTG SEQ.ID.NO:1755	-1.3	-16.6	53.8	-15.3	0	-3.7
338	CCATCCAAATTTTTCAATTG SEQ.ID.NO:1756	-1.2	-19.3	57.6	-17.4	-0.5	-6.1
453	TTCTGTCCCAGAGGACCTGC SEQ.ID.NO:1757	-1.2	-29	81.2	-24.8	-3	-8.2
559	CTGGGGGTAGAAACCCAGGT SEQ.ID.NO:1758	-1.2	-27.1	74.6	-21.8	-4.1	-9.8
589	TATTCCAGGAGAGTACCACT	-1.2	-24.2	70.6	-22.1	-0.5	-8.9

position	oligo	kcal/ mol total binding	kcal/ mol duplex formation	deg C Tm of Duplex	kcal/ mol target structure	kcal/ mol Intra-molecular oligo	kcal/ mol Inter-molecular oligo
	SEQ.ID.NO:1759						
623	AGAGAGTCTCAGCTGGCATA SEQ.ID.NO:1760	-1.2	-24.9	74.9	-22.3	-1.1	-10
748	GTGGTATCCAGAGGCTCTGT SEQ.ID.NO:1761	-1.2	-27.4	81	-24.6	-1.5	-8
1191	ATGAGAAAATTTTCTTCTGC SEQ.ID.NO:1762	-1.2	-17.9	56.4	-14.5	-1	-12.5
1242	TTTGTGAATTCTACAAGAAC SEQ.ID.NO:1763	-1.2	-16.7	53.6	-14.1	-0.9	-10.5
1469	GAGTCATTTTCAGTTCCCCA SEQ.ID.NO:1764	-1.2	-26.7	77.2	-25.5	0	-4.1
2024	GATAGAATTGAAGTAACAAT SEQ.ID.NO:1765	-1.1	-14.6	48.7	-12.6	-0.7	-4.2
28	GGATAAGTCGGGGAGACAAT SEQ.ID.NO:1766	-1	-22.2	64.3	-19.1	-2.1	-5.5
263	CATCTTGAGGAAATGTCCAG SEQ.ID.NO:1767	-1	-21.4	63.4	-18.3	-2.1	-5.7
289	AAAAAACTCCAAAGTGTCTG SEQ.ID.NO:1768	-1	-17	52.8	-16	0	-3
290	AAAAAAACTCCAAAGTGTCT SEQ.ID.NO:1769	-1	-16.3	51.2	-14.6	-0.5	-3
472	GTATGGTTCCACTTCCAGGT SEQ.ID.NO:1770	-1	-27.2	79	-25.3	-0.7	-5.6
518	AAATCTGTGGTTGAACTTGG SEQ.ID.NO:1771	-1	-19.9	60.3	-18.9	0	-3.4
798	ATGCTTCTCCTGAAGAAACC SEQ.ID.NO:1772	-1	-22.7	65.2	-19.5	-2.2	-5.7
1075	TGGGGTGAGTTCAGTTTTCT SEQ.ID.NO:1773	-1	-24.6	75.3	-23.6	0	-2.9
1165	TTCTTCTTTTAAAATTTTAT SEQ.ID.NO:1774	-1	-14.7	49.9	-13.2	0	-8
1167	AATTCTTCTTTTAAAATTTT SEQ.ID.NO:1775	-1	-14.3	48.8	-13.3	0	-6.5
1499	CAATTGCTGTAAGCAGAGCA SEQ.ID.NO:1776	-1	-22.6	66.2	-18.5	-3.1	-10.6
1500	ACAATTGCTGTAAGCAGAGC SEQ.ID.NO:1777	-1	-22.1	65.5	-18.3	-2.8	-9
1644	AGGCGACCCAGGAGACAGGC SEQ.ID.NO:1778	-1	-29.6	79.5	-27.6	-0.9	-5.4
2025	AGATAGAATTGAAGTAACAA SEQ.ID.NO:1779	-1	-14.6	48.8	-13.6	0	-3.3
2030	TCAACAGATAGAATTGAAGT SEQ.ID.NO:1780	-1	-16.7	53.5	-15.1	-0.3	-4.1
191	AGTCTTCTTTTCTTCTTTCA SEQ.ID.NO:1781	-0.9	-22.2	70.9	-21.3	0	-1.5
192	AAGTCTTCTTTTCTTCTTTC SEQ.ID.NO:1782	-0.9	-20.8	66.9	-19.9	0	-2.4
246	CAGAAGAAATCCAGGAAACT SEQ.ID.NO:1783	-0.9	-18.4	55.4	-17	-0.2	-5.7
397	AAAAGAAAATTCATCTGTGG SEQ.ID.NO:1784	-0.9	-15.3	49.8	-14.4	0	-4.8
498	GGAAACTGAACATTGCTGTA SEQ.ID.NO:1785	-0.9	-20	59.7	-18.4	-0.5	-3.9
590	ATATTCCAGGAGAGTACCAC SEQ.ID.NO:1786	-0.9	-23.3	68.6	-21.7	-0.5	-5.3

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intra-molecular oligo	kcal/mol Inter-molecular oligo
636	GTTTCTCCCTGGTAGAGAGT SEQ.ID.NO:1787	-0.9	-26.5	79	-24.5	-1	-7
1327	ACGAAGGAACATAGCTTCAA SEQ.ID.NO:1788	-0.9	-19.8	58.6	-16.9	-2	-5.6
1341	AAAATCTCAGCTGAACGAAG SEQ.ID.NO:1789	-0.9	-17.8	54.3	-15.8	0	-10.1
1512	GGAGACAGGATAACAATTGC SEQ.ID.NO:1790	-0.9	-20.2	60.5	-19.3	0	-7
1825	AATAAAGGAAAGTTATACAT SEQ.ID.NO:1791	-0.9	-13.6	46.6	-12.7	0	-2.8
286	AAACTCCAAAGTGTCTGAAG SEQ.ID.NO:1792	-0.8	-19	57.6	-17.5	-0.5	-5
533	AATAGGATGACGAGGAAATC SEQ.ID.NO:1793	-0.8	-17.8	54.7	-17	0	-3.5
638	CAGTTTCTCCCTGGTAGAGA SEQ.ID.NO:1794	-0.8	-26	76.4	-24.5	-0.5	-6.3
1195	CAAAATGAGAAAATTTTCTT SEQ.ID.NO:1795	-0.8	-13.4	46	-10.4	-1	-12.5
1881	GTAATTACAACATAAATATT SEQ.ID.NO:1796	-0.8	-13.2	45.9	-11.9	0	-8.1
69	AGCGATTTTGCTACAAATGC SEQ.ID.NO:1797	-0.7	-21.2	61.9	-18.9	-1.5	-8
337	CATCCAAATTTTTCAATTGA SEQ.ID.NO:1798	-0.7	-17.9	55.2	-16.5	-0.5	-8.1
633	TCTCCCTGGTAGAGAGTCTC SEQ.ID.NO:1799	-0.7	-26.8	80.4	-25.2	-0.7	-8.7
951	TTAGATTTACACTGAATTTC SEQ.ID.NO:1800	-0.7	-16.8	54.5	-16.1	0	-3.8
1497	ATTGCTGTAAGCAGAGCATA SEQ.ID.NO:1801	-0.7	-22.3	66.6	-18.5	-3.1	-10.7
1556	GAAGCTTCTCTACTGCCTCT SEQ.ID.NO:1802	-0.7	-26.1	76.2	-24.4	0	-10
154	TCTACCTCCTTGGATTGTTT SEQ.ID.NO:1803	-0.6	-24.8	72.5	-23.5	-0.5	-4.6
593	CATATATTCCAGGAGAGTAC SEQ.ID.NO:1804	-0.6	-20.8	63.5	-20.2	0	-5.3
728	CTCCACAAACAACACACAGC SEQ.ID.NO:1805	-0.6	-22.2	63	-21.6	0	-2.8
1414	TTCATCAGAGATACCACTAT SEQ.ID.NO:1806	-0.6	-20.9	63.3	-20.3	0	-3.5
1439	AAAAACTAAACATAGGTGTT SEQ.ID.NO:1807	-0.6	-14.9	49	-12.7	-1.5	-5.5
1626	GCAAAGTGTTGAGGATTTTC SEQ.ID.NO:1808	-0.6	-20.7	63.4	-19.2	-0.7	-3.4
1879	AATTACAACATAAATATTCA SEQ.ID.NO:1809	-0.6	-13.4	46.2	-12.8	0	-4.6
252	AATGTCCAGAAGAAATCCAG SEQ.ID.NO:1810	-0.5	-19.8	58.8	-19.3	0	-2.2
532	ATAGGATGACGAGGAAATCT SEQ.ID.NO:1811	-0.5	-19.4	58.3	-18.4	-0.1	-3.5
859	CATGTACATATCCATCACAC SEQ.ID.NO:1812	-0.5	-21.5	64	-20.5	0	-8
1074	GGGGTGAGTTCAGTTTTCTC SEQ.ID.NO:1813	-0.5	-25	77.5	-24.5	0	-3.4
1168	GAATTCTTCTTTTAAAATTT	-0.5	-14.8	49.7	-14.3	0	-6.3

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intra-molecular oligo	kcal/mol Inter-molecular oligo
	SEQ.ID.NO:1814						
1520	GTCTATCTGGAGACAGGATA SEQ.ID.NO:1815	-0.5	-22.3	68	-19.4	-2.4	-9.5
1993	GGCAAACAGGGCTTGCCAAT SEQ.ID.NO:1816	-0.5	-26.2	71.2	-22	-3.7	-10.4
721	AACAACACACAGCTCATCCC SEQ.ID.NO:1817	-0.4	-24.4	68.2	-24	0	-4.4
749	AGTGGTATCCAGAGGCTCTG SEQ.ID.NO:1818	-0.4	-26.2	77.5	-24.5	-1.2	-7.6
828	TTTTTACACTTGTACACAGC SEQ.ID.NO:1819	-0.4	-20.7	63.5	-20.3	0	-6.3
938	GAATTTCAGTTAACAAGCAT SEQ.ID.NO:1820	-0.4	-18.2	56.6	-17.8	0	-7.3
952	CTTAGATTTACACTGAATTT SEQ.ID.NO:1821	-0.4	-17.3	55.2	-16.9	0	-3.8
1506	AGGATAACAATTGCTGTAAG SEQ.ID.NO:1822	-0.4	-18	56	-16.9	-0.4	-7
1517	TATCTGGAGACAGGATAACA SEQ.ID.NO:1823	-0.4	-20	60.8	-17.2	-2.4	-9.5
78	CCAGATCCCAGCGATTTTGC SEQ.ID.NO:1824	-0.3	-27.7	74.9	-26.5	-0.7	-5.9
193	TAAGTCTTCTTTTCTTCTTT SEQ.ID.NO:1825	-0.3	-20.1	64.5	-19.2	-0.3	-3
370	ATGGGAATGTTCAATGAGAT SEQ.ID.NO:1826	-0.3	-19.2	58.7	-18.9	0	-5.7
634	TTCTCCCTGGTAGAGAGTCT SEQ.ID.NO:1827	-0.3	-26.5	78.8	-25.1	-1	-7
773	ACCCCTCACAGGTCAGTGCA SEQ.ID.NO:1828	-0.3	-30.3	83.7	-29.3	-0.5	-6
789	CTGAAGAAACCTTTACACCC SEQ.ID.NO:1829	-0.3	-22.1	62.4	-21.8	0	-2.8
1735	TTCACAGAGAAGTGGGGTAA SEQ.ID.NO:1830	-0.3	-21.6	64.9	-20.4	-0.7	-4.6
2081	AATAAAATATATGCAATATG SEQ.ID.NO:1831	-0.3	-11.8	42.9	-10.8	-0.5	-6.5
77	CAGATCCCAGCGATTTTGCT SEQ.ID.NO:1832	-0.2	-26.6	73.4	-24.8	-1.5	-7.4
635	TTTCTCCCTGGTAGAGAGTC SEQ.ID.NO:1833	-0.2	-25.7	77.1	-24.4	-1	-7
720	ACAACACACAGCTCATCCCC SEQ.ID.NO:1834	-0.2	-27.1	73.8	-26.9	0	-4.4
778	TTTACACCCCTCACAGGTCA SEQ.ID.NO:1835	-0.2	-27.4	76.4	-26.5	-0.5	-3.9
801	GTAATGCTTCTCCTGAAGAA SEQ.ID.NO:1836	-0.2	-21.4	63.5	-19	-2.2	-6.7
1407	GAGATACCACTATTTCGAAT SEQ.ID.NO:1837	-0.2	-19.9	59.4	-19.7	0	-6.7
1633	GAGACAGGCAAAGTGTTGAG SEQ.ID.NO:1838	-0.2	-21.5	64.5	-20.4	-0.7	-4
247	CCAGAAGAAATCCAGGAAAC SEQ.ID.NO:1839	-0.1	-19.5	57.1	-19.4	0	-5.7
426	TCTGTTAAAACACCAAATAA SEQ.ID.NO:1840	-0.1	-15.6	49.9	-15.5	0	-5.5
829	GTTTTTACACTTGTACACAG SEQ.ID.NO:1841	-0.1	-20.1	62.5	-20	0	-6.2

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intra-molecular oligo	kcal/mol Inter-molecular oligo
1462	TTTCAGTTCCCCAATACTTT SEQ.ID.NO:1842	-0.1	-24	69.2	-23.9	0	-2.9
1494	GCTGTAAGCAGAGCATACTC SEQ.ID.NO:1843	-0.1	-23.7	70.7	-20.4	-3.2	-8.2
1524	TATTGTCTATCTGGAGACAG SEQ.ID.NO:1844	-0.1	-20.6	64.1	-18.2	-2.3	-7.8
15	AGACAATGAGGTGAGGAGGA SEQ.ID.NO:1845	0	-22	65.5	-22	0	-3.1
1515	TCTGGAGACAGGATAACAAT SEQ.ID.NO:1846	0	-19.6	59.4	-17.2	-2.4	-9.5
1516	ATCTGGAGACAGGATAACAA SEQ.ID.NO:1847	0	-19.6	59.4	-17.2	-2.4	-9.5
1559	CCTGAAGCTTCTCTACTGCC SEQ.ID.NO:1848	0	-26.8	75.9	-25.4	0	-10.8
1877	TTACAACATAAATATTCATC SEQ.ID.NO:1849	0	-14.5	48.8	-14.5	0	-4.6
27	GATAAGTCGGGGAGACAATG SEQ.ID.NO:1850	0.1	-21	61.7	-19.7	-1.3	-4.5
188	CTTCTTTTCTTCTTTCACTC SEQ.ID.NO:1851	0.1	-22.1	69.7	-22.2	0	0
939	TGAATTTCAGTTAACAAGCA SEQ.ID.NO:1852	0.1	-18.2	56.6	-18.3	0	-7.3
1186	AAAATTTTCTTCTGCACTGA SEQ.ID.NO:1853	0.1	-19.1	58.6	-19.2	0	-6.3
1871	CATAAATATTCATCAAGATT SEQ.ID.NO:1854	0.1	-15	49.7	-15.1	0	-4.6
19	GGGGAGACAATGAGGTGAGG SEQ.ID.NO:1855	0.2	-23.8	69.1	-24	0	-3.1
245	AGAAGAAATCCAGGAAACTA SEQ.ID.NO:1856	0.2	-17.4	53.7	-17	-0.3	-5.7
541	GTTGGAATAATAGGATGACG SEQ.ID.NO:1857	0.2	-18.5	56.3	-18.7	0	-3
544	CAGGTTGGAATAATAGGATG SEQ.ID.NO:1858	0.2	-18.8	57.7	-19	0	-1.6
1099	AAAATGTAGAAGAGTCTGTT SEQ.ID.NO:1859	0.2	-17.1	54.9	-16.8	-0.2	-5.8
1190	TGAGAAAATTTTCTTCTGCA SEQ.ID.NO:1860	0.2	-18.6	57.7	-16.6	-1	-12.5
1503	ATAACAATTGCTGTAAGCAG SEQ.ID.NO:1861	0.2	-18.7	57.4	-15.8	-3.1	-7.9
1513	TGGAGACAGGATAACAATTG SEQ.ID.NO:1862	0.2	-18.4	56.5	-17.9	-0.4	-7.4
1736	TTTCACAGAGAAGTGGGGTA SEQ.ID.NO:1863	0.2	-22.4	67.6	-21.7	-0.7	-4.8
463	CACTTCCAGGTTCTGTCCCA SEQ.ID.NO:1864	0.3	-29.1	81.8	-28.9	-0.2	-3.7
756	GCATTATAGTGGTATCCAGA SEQ.ID.NO:1865	0.3	-23	68.9	-22.5	-0.6	-6.9
1357	CGGAAGTTTCTTATTGAAAA SEQ.ID.NO:1866	0.3	-17	53.2	-15.8	-1.4	-6.6
1406	AGATACCACTATTTCGAATT SEQ.ID.NO:1867	0.3	-19.4	58.5	-19.7	0	-6.7
1409	CAGAGATACCACTATTTCGA SEQ.ID.NO:1868	0.3	-21.3	62.7	-20.9	-0.5	-5.5
1440	TAAAAACTAAACATAGGTGT	0.3	-14.5	48.2	-14.1	-0.5	-3.5

position	oligo	kcal/ mol total binding	kcal/ mol duplex forma- tion	deg C Tm of Duplex	kcal/ mol target struc- ture	kcal/ mol Intra- mole- cular oligo	kcal/ mol Inter- mole- cular oligo
	SEQ.ID.NO:1869 TGAAGCTTCTCTACTGCCTC						
1557	SEQ.ID.NO:1870 TAAAGGAAAGTTATACATCA	0.3	-25.2	73.9	-24.1	0	-10.8
1823	SEQ.ID.NO:1871 GAGGAAATGTCCAGAAGAAA	0.3	-15.4	50.5	-15.7	0	-2.6
257	SEQ.ID.NO:1872 ATCCAAATTTTTCAATTGAA	0.4	-18.4	55.8	-16.7	-2.1	-4.9
336	SEQ.ID.NO:1873 GAAAAAGAAAATTCATCTGT	0.4	-16.5	52.3	-15.8	0	-10.1
399	SEQ.ID.NO:1874 CTTCCAGGTTCTGTCCCAGA	0.4	-14	47.2	-14.4	0	-4.8
461	SEQ.ID.NO:1875 AATCTGTGGTTGAACTTGGG	0.4	-28.8	81.9	-28.1	-1	-5.3
517	SEQ.ID.NO:1876 GAATAATAGGATGACGAGGA	0.4	-21.8	65	-22.2	0	-3.4
537	SEQ.ID.NO:1877 ATTCCAGGAGAGTACCACTC	0.4	-18.4	55.9	-18.8	0	-3.5
588	SEQ.ID.NO:1878 TCAGTTTCTCCCTGGTAGAG	0.4	-24.9	72.9	-23.8	-1.4	-8.5
639	SEQ.ID.NO:1879 TTACACCCCTCACAGGTCAG	0.4	-25.8	76.8	-25.7	-0.2	-4.6
777	SEQ.ID.NO:1880 GCATGTACATATCCATCACA	0.4	-27.3	76.4	-27	-0.5	-4.1
860	SEQ.ID.NO:1881 TGTAAGCAGAGCATACTCCT	0.4	-23.1	67.6	-23	0	-8
1492	SEQ.ID.NO:1882 TAAATATTCATCAAGATTTC	0.4	-23.9	70	-22.8	-1.4	-6.4
1869	SEQ.ID.NO:1883 ATCTGTGGTAGGTAAATGGG	0.4	-14.8	49.8	-15.2	3.8	-4.6
385	SEQ.ID.NO:1884 AACACACAGCTCATCCCCTT	0.5	-21.7	65.4	-22.2	0	-1.9
718	SEQ.ID.NO:1885 TTTACACTGAATTTCAGTTA	0.5	-27.2	74.4	-27.7	0	-4.4
946	SEQ.ID.NO:1886 AGAGATACCACTATTTCGAA	0.5	-18.1	57.5	-16.3	-2.3	-11.1
1408	SEQ.ID.NO:1887 CACAGAGAAGTGGGGTAAAC	0.5	-19.9	59.6	-19.7	-0.5	-6.5
1733	SEQ.ID.NO:1888 GGGTAGAAACCCAGGTTGGA	0.5	-20.6	61.5	-20.6	-0.1	-4.2
555	SEQ.ID.NO:1889 ATTTTCTTCTGCACTGAATT	0.6	-25.7	71.8	-23	-3.3	-8.9
1183	SEQ.ID.NO:1890 CCAATACTTTTATAAAAACT	0.6	-20.6	63.1	-21.2	0	-4.9
1452	SEQ.ID.NO:1891 CAATTTAATTAGGCAAACAG	0.6	-14.8	48.5	-14.9	0	-7.8
2004	SEQ.ID.NO:1892 GGTCTTCAAAAAAAACTCCA	0.6	-16.2	51.6	-16.8	0	-4
298	SEQ.ID.NO:1893 CCACTTCCAGGTTCTGTCCC	0.7	-18.2	55	-18.9	0	-2.8
464	SEQ.ID.NO:1894 GTAGAAACCCAGGTTGGAAT	0.7	-30.4	84.3	-30.6	-0.2	-3.7
553	SEQ.ID.NO:1895 TTTATAAAAACTAAACATAG	0.7	-22.6	64.7	-22.4	-0.8	-6.5
1444	SEQ.ID.NO:1896	0.7	-10.8	41.2	-11.5	0	-5.5

position	oligo	kcal/ mol total binding	kcal/ mol duplex formation	deg C Tm of Duplex	kcal/ mol target structure	kcal/ mol Intra-molecular oligo	kcal/ mol Inter-molecular oligo
1696	CCATGACATCAGCATCTCAG SEQ.ID.NO:1897	0.7	-24.2	70.3	-24.9	0	-4.5
1737	ATTTCACAGAGAAGTGGGGT SEQ.ID.NO:1898	0.7	-22.7	68.1	-22.5	-0.7	-4.8
1826	AAATAAAGGAAAGTTATACA SEQ.ID.NO:1899	0.7	-12.9	45.1	-13.6	0	-2.8
4	TGAGGAGGAGGAGAGAGTCT SEQ.ID.NO:1900	0.8	-23.7	71.9	-24.5	0	-5.7
189	TCTTCTTTTCTTCTTTCACT SEQ.ID.NO:1901	0.8	-22.1	69.7	-22.9	0	0
255	GGAAATGTCCAGAAGAAATC SEQ.ID.NO:1902	0.8	-18.2	55.6	-17.6	-1.3	-4.4
288	AAAAACTCCAAAGTGTCTGA SEQ.ID.NO:1903	0.8	-18.3	55.7	-18.4	-0.5	-3.6
947	ATTTACACTGAATTTCAGTT SEQ.ID.NO:1904	0.8	-18.4	58.1	-16.7	-2.5	-11.3
1022	GCAAGTCACGACCTTCACTG SEQ.ID.NO:1905	0.8	-25.1	70.7	-25.9	0	-4.7
1098	AAATGTAGAAGAGTCTGTTG SEQ.ID.NO:1906	0.8	-17.8	56.8	-18.1	-0.2	-5.8
1326	CGAAGGAACATAGCTTCAAC SEQ.ID.NO:1907	0.8	-19.8	58.6	-18.6	-2	-5.6
1420	TATATATTCATCAGAGATAC SEQ.ID.NO:1908	0.8	-16.5	54.3	-17.3	0	-3.9
1461	TTCAGTTCCCCAATACTTTT SEQ.ID.NO:1909	0.8	-24	69.2	-24.8	0	-2.9
1885	ACATGTAATTACAACATAAA SEQ.ID.NO:1910	0.8	-14.3	47.8	-13.8	-0.6	-10.3
281	CCAAAGTGTCTGAAGTTTCA SEQ.ID.NO:1911	0.9	-21.4	64	-22.3	0	-4.5
502	TTGGGGAAACTGAACATTGC SEQ.ID.NO:1912	0.9	-20.7	60.7	-21.1	-0.2	-2.9
1089	AGAGTCTGTTGATCTGGGGT SEQ.ID.NO:1913	0.9	-25.1	76.3	-26	0	-5
398	AAAAAGAAAATTCATCTGTG SEQ.ID.NO:1914	1	-13.4	46	-14.4	0	-4.6
473	AGTATGGTTCCACTTCCAGG SEQ.ID.NO:1915	1	-26	75.6	-26.1	-0.7	-5.6
499	GGGAAACTGAACATTGCTGT SEQ.ID.NO:1916	1	-21.5	62.7	-21.8	-0.5	-4
729	TCTCCACAAACAACACACAG SEQ.ID.NO:1917	1	-20.8	60.5	-21.8	0	-1.3
1405	GATACCACTATTTCGAATTC SEQ.ID.NO:1918	1	-19.8	59.6	-20.8	0	-6.7
1872	ACATAAATATTCATCAAGAT SEQ.ID.NO:1919	1	-15.1	49.9	-16.1	0	-4.1
450	TGTCCCAGAGGACCTGCCAC SEQ.ID.NO:1920	1.1	-30.5	82.1	-28.6	-3	-8.6
552	TAGAAACCCAGGTTGGAATA SEQ.ID.NO:1921	1.1	-21.1	61.3	-21.3	-0.8	-7
727	TCCACAAACAACACACAGCT SEQ.ID.NO:1922	1.1	-22.2	63	-23.3	0	-4.3
1200	TCCGTCAAAATGAGAAAATT SEQ.ID.NO:1923	1.1	-16.6	51.4	-17.2	-0.1	-3.2
1445	TTTTATAAAAACTAAACATA	1.1	-10.9	41.4	-11.5	0	-7.5

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intra-molecular oligo	kcal/mol Inter-molecular oligo
	SEQ.ID.NO:1924						
	GTATTGTCTATCTGGAGACA						
1525	SEQ.ID.NO:1925	1.1	-21.8	67.3	-20.8	-2.1	-9.3
	TCCATGACATCAGCATCTCA						
1697	SEQ.ID.NO:1926	1.1	-24.6	71.7	-25.7	0	-4.5
	ACCAAATAAATTTTCAGAAA						
415	SEQ.ID.NO:1927	1.2	-14.4	47.6	-15.6	0	-5.3
	TTTACTCTCCATGACATCAG						
1704	SEQ.ID.NO:1928	1.2	-22	66.1	-23.2	0	-4.5
	AATTTAATTAGGCAAACAGG						
2003	SEQ.ID.NO:1929	1.2	-16.7	52.7	-17.9	0	-4.1
	AAATGTCCAGAAGAAATCCA						
253	SEQ.ID.NO:1930	1.3	-19.1	56.8	-20.4	0	-2.2
	AATGGGAATGTTCAATGAGA						
371	SEQ.ID.NO:1931	1.3	-18.5	56.8	-19.8	0	-4.9
	CTTGGGGAAACTGAACATTG						
503	SEQ.ID.NO:1932	1.3	-19.8	58.7	-21.1	0.6	-2.3
	CCTCAGTTTCTCCCTGGTAG						
641	SEQ.ID.NO:1933	1.3	-28.1	80.9	-28.9	-0.2	-4.2
	GAAGAGTCTGTTGATCTGGG						
1091	SEQ.ID.NO:1934	1.3	-22.6	68.6	-23.4	-0.1	-5.8
	ATATATTCATCAGAGATACC						
1419	SEQ.ID.NO:1935	1.3	-18.8	58.9	-20.1	0	-3.6
	CTCTCCATGACATCAGCATC						
1700	SEQ.ID.NO:1936	1.3	-24.8	72.5	-26.1	0	-4.1
	GGAGGAGGAGAGAGTCTCGT						
1	SEQ.ID.NO:1937	1.4	-25.5	75.7	-24.5	-2.4	-10
	TGGGAGGATTCTGGACTGAG						
107	SEQ.ID.NO:1938	1.4	-23.7	69.9	-25.1	0	-2.9
	AAAAAAAACTCCAAAGTGTC						
291	SEQ.ID.NO:1939	1.4	-14.7	48.1	-15.4	-0.5	-3
	TGGTCTTCAAAAAAAACTCC						
299	SEQ.ID.NO:1940	1.4	-17.5	53.8	-18.9	0	-2.5
	CCAAATAAATTTTCAGAAAA						
414	SEQ.ID.NO:1941	1.4	-13.5	45.8	-14.4	-0.1	-7.7
	ACAGCTCATCCCCTTTGATC						
713	SEQ.ID.NO:1942	1.4	-27.2	76.7	-28.6	0	-4.4
	CCGTCAAAATGAGAAAATTT						
1199	SEQ.ID.NO:1943	1.4	-16.3	50.7	-17.2	-0.1	-5
	AAGTTTCTTATTGAAAATCT						
1354	SEQ.ID.NO:1944	1.4	-15.7	51.7	-15.6	-1.4	-4.5
	CAAAGTGTCTGAAGTTTCAT						
280	SEQ.ID.NO:1945	1.5	-19.4	60.2	-20.9	0	-4.7
	TGACGAGGAAATCTGTGGTT						
526	SEQ.ID.NO:1946	1.5	-21.6	63.4	-23.1	0	-3.5
	AGAAACCCAGGTTGGAATAA						
551	SEQ.ID.NO:1947	1.5	-20.7	59.9	-21.3	-0.8	-7
	TGTACATATCCATCACACAG						
857	SEQ.ID.NO:1948	1.5	-21.5	64.2	-23	0	-5.9
	TTTTCTTCTGCACTGAATTC						
1182	SEQ.ID.NO:1949	1.5	-21	64.6	-22.5	0	-5.9
	AATTTTCTTCTGCACTGAAT						
1184	SEQ.ID.NO:1950	1.5	-19.8	60.6	-21.3	0	-4.9
	GTACAAGTGAAATAAAGGAA						
1835	SEQ.ID.NO:1951	1.5	-14.9	49	-16.4	0	-4.6

position	oligo	kcal/ mol total binding	kcal/ mol duplex forma- tion	deg C Tm of Duplex	kcal/ mol target struc- ture	kcal/ mol Intra- mole- cular oligo	kcal/ mol Inter- mole- cular oligo
1876	TACAACATAAATATTCATCA SEQ.ID.NO:1952	1.5	-15.1	49.8	-16.6	0	-4.6
14	GACAATGAGGTGAGGAGGAG SEQ.ID.NO:1953	1.6	-22	65.5	-23.6	0	-3.1
262	ATCTTGAGGAAATGTCCAGA SEQ.ID.NO:1954	1.6	-21.3	63.5	-20.8	-2.1	-6.6
404	TTTCAGAAAAAGAAAATTCA SEQ.ID.NO:1955	1.6	-12.8	44.9	-13.8	-0.3	-5.1
416	CACCAAATAAATTTTCAGAA SEQ.ID.NO:1956	1.6	-15.8	50.3	-17.4	0	-4.7
766	ACAGGTCAGTGCATTATAGT SEQ.ID.NO:1957	1.6	-22.8	69.9	-24.4	0	-5.4
259	TTGAGGAAATGTCCAGAAGA SEQ.ID.NO:1958	1.7	-19.9	59.7	-19.5	-2.1	-5.2
767	CACAGGTCAGTGCATTATAG SEQ.ID.NO:1959	1.7	-22.3	67.6	-24	0	-5.4
1451	CAATACTTTTATAAAAACTA SEQ.ID.NO:1960	1.7	-12.5	44.4	-13.7	0	-7.8
1822	AAAGGAAAGTTATACATCAG SEQ.ID.NO:1961	1.7	-15.7	51.2	-17.4	0	-2.9
287	AAAACTCCAAAGTGTCTGAA SEQ.ID.NO:1962	1.8	-18.3	55.7	-19.4	-0.5	-5
640	CTCAGTTTCTCCCTGGTAGA SEQ.ID.NO:1963	1.8	-26.7	78.5	-28	-0.2	-4.2
943	ACACTGAATTTCAGTTAACA SEQ.ID.NO:1964	1.8	-18.4	57.3	-17.7	-2.5	-11.3
16	GAGACAATGAGGTGAGGAGG SEQ.ID.NO:1965	1.9	-22	65.5	-23.9	0	-3.1
405	TTTTCAGAAAAAGAAAATTC SEQ.ID.NO:1966	1.9	-12.2	43.9	-12.7	-1.3	-7.1
406	ATTTTCAGAAAAAGAAAATT SEQ.ID.NO:1967	1.9	-11.8	43	-11.5	-2.2	-8.1
516	ATCTGTGGTTGAACTTGGGG SEQ.ID.NO:1968	1.9	-23.7	69.9	-25.6	0	-3.4
542	GGTTGGAATAATAGGATGAC SEQ.ID.NO:1969	1.9	-18.9	58.1	-20.8	0	-2
722	AAACAACACACAGCTCATCC SEQ.ID.NO:1970	1.9	-21.7	62.7	-23.6	0	-4.4
786	AAGAAACCTTTACACCCCTC SEQ.ID.NO:1971	1.9	-23.9	66	-25.8	0	-2.4
1100	TAAAATGTAGAAGAGTCTGT SEQ.ID.NO:1972	1.9	-16.7	54	-18.1	-0.2	-5.8
1170	CTGAATTCTTCTTTTAAAAT SEQ.ID.NO:1973	1.9	-15.5	51	-16.7	-0.4	-6.9
1180	TTCTTCTGCACTGAATTCTT SEQ.ID.NO:1974	1.9	-21.8	66.3	-23.7	0	-6.9
1181	TTTCTTCTGCACTGAATTCT SEQ.ID.NO:1975	1.9	-21.8	66.3	-23.7	0	-6.9
1325	GAAGGAACATAGCTTCAACC SEQ.ID.NO:1976	1.9	-21	61.7	-21.3	-1.5	-5.4
1441	ATAAAAACTAAACATAGGTG SEQ.ID.NO:1977	1.9	-13.3	45.8	-15.2	0	-3.5
190	GTCTTCTTTTCTTCTTTCAC SEQ.ID.NO:1978	2	-22.4	71.2	-24.4	0	-0.8
194	CTAAGTCTTCTTTTCTTCTT	2	-20.9	66.3	-22.3	-0.3	-3

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intramolecular oligo	kcal/mol Intermolecular oligo
	SEQ.ID.NO:1979						
540	TTGGAATAATAGGATGACGA SEQ.ID.NO:1980	2	-17.9	54.8	-19.9	0	-3.5
550	GAAACCCAGGTTGGAATAAT SEQ.ID.NO:1981	2	-20.7	59.7	-22.1	-0.3	-7
726	CCACAAACAACACACAGCTC SEQ.ID.NO:1982	2	-22.2	63	-24.2	0	-4.4
776	TACACCCCTCACAGGTCAGT SEQ.ID.NO:1983	2	-28.4	79.5	-29.7	-0.5	-4.1
1169	TGAATTCTTCTTTTAAAATT SEQ.ID.NO:1984	2	-14.7	49.4	-16	-0.4	-6.9
1496	TTGCTGTAAGCAGAGCATAC SEQ.ID.NO:1985	2	-22.5	67.2	-21.4	-3.1	-10.7
1698	CTCCATGACATCAGCATCTC SEQ.ID.NO:1986	2	-24.8	72.5	-26.8	0	-4.5
1734	TCACAGAGAAGTGGGGTAAA SEQ.ID.NO:1987	2	-20.8	62.4	-21.9	-0.7	-4.6
1836	GGTACAAGTGAAATAAAGGA SEQ.ID.NO:1988	2	-16.8	52.9	-18.8	0	-5.2
527	ATGACGAGGAAATCTGTGGT SEQ.ID.NO:1989	2.1	-21.5	63.1	-23.6	0	-3.5
557	GGGGGTAGAAACCCAGGTTG SEQ.ID.NO:1990	2.1	-26.3	73.1	-24.3	-4.1	-9.1
783	AAACCTTTACACCCCTCACA SEQ.ID.NO:1991	2.1	-25.6	69.2	-27.7	0	-1.4
1090	AAGAGTCTGTTGATCTGGGG SEQ.ID.NO:1992	2.1	-23.2	69.9	-24.8	-0.1	-5.8
1198	CGTCAAAATGAGAAAATTTT SEQ.ID.NO:1993	2.1	-14.4	47.5	-15.8	-0.5	-7.2
1418	TATATTCATCAGAGATACCA SEQ.ID.NO:1994	2.1	-19.5	60.2	-21.6	0	-3.5
1884	CATGTAATTACAACATAAAT SEQ.ID.NO:1995	2.1	-14.1	47.4	-14.9	-0.6	-10.3
261	TCTTGAGGAAATGTCCAGAA SEQ.ID.NO:1996	2.3	-20.6	61.5	-20.8	-2.1	-6.3
548	AACCCAGGTTGGAATAATAG SEQ.ID.NO:1997	2.3	-20.5	60	-21.9	-0.8	-6.1
549	AAACCCAGGTTGGAATAATA SEQ.ID.NO:1998	2.3	-19.8	58.1	-21.2	-0.8	-7
584	CAGGAGAGTACCACTCTTCA SEQ.ID.NO:1999	2.3	-24.5	72.3	-23.4	-3.4	-8.6
785	AGAAACCTTTACACCCCTCA SEQ.ID.NO:2000	2.3	-25.3	69.1	-27.6	0	-2.5
1189	GAGAAAATTTTCTTCTGCAC SEQ.ID.NO:2001	2.3	-18.8	58.3	-18.9	-1	-12.5
6	GGTGAGGAGGAGGAGAGAGT SEQ.ID.NO:2002	2.4	-24.8	74.5	-27.2	0	0
269	AAGTTTCATCTTGAGGAAAT SEQ.ID.NO:2003	2.4	-18.2	57.1	-19.7	-0.7	-7.9
297	GTCTTCAAAAAAAACTCCAA SEQ.ID.NO:2004	2.4	-16.3	51.2	-18.7	0	-1.9
530	AGGATGACGAGGAAATCTGT SEQ.ID.NO:2005	2.4	-20.9	61.6	-22.8	-0.1	-3.5
637	AGTTTCTCCCTGGTAGAGAG SEQ.ID.NO:2006	2.4	-25.3	75.5	-26.6	-1	-7

position	oligo	kcal/ mol total binding	kcal/ mol duplex forma- tion	deg C Tm of Duplex	kcal/ mol target struc- ture	kcal/ mol Intra- mole- cular oligo	kcal/ mol Inter- mole- cular oligo
1449	ATACTTTTATAAAAACTAAA SEQ.ID.NO:2007	2.4	-11.1	41.8	-13	0	-7.8
400	AGAAAAAGAAAATTCATCTG SEQ.ID.NO:2008	2.5	-12.8	44.9	-14.4	-0.7	-4.8
514	CTGTGGTTGAACTTGGGGAA SEQ.ID.NO:2009	2.5	-23.2	67.3	-25.7	0	-3.1
531	TAGGATGACGAGGAAATCTG SEQ.ID.NO:2010	2.5	-19.4	58.2	-21.4	-0.1	-3.5
558	TGGGGGTAGAAACCCAGGTT SEQ.ID.NO:2011	2.5	-26.3	73.1	-24.7	-4.1	-9
1703	TTACTCTCCATGACATCAGC SEQ.ID.NO:2012	2.5	-23.7	70.1	-26.2	0	-4.5
1518	CTATCTGGAGACAGGATAAC SEQ.ID.NO:2013	2.6	-20.2	61.5	-20.4	-2.4	-9.5
1701	ACTCTCCATGACATCAGCAT SEQ.ID.NO:2014	2.6	-24.6	71.4	-27.2	0	-4.5
505	AACTTGGGGAAACTGAACAT SEQ.ID.NO:2015	2.7	-19.2	57.2	-21.4	-0.2	-2.5
1495	TGCTGTAAGCAGAGCATACT SEQ.ID.NO:2016	2.7	-23.3	68.9	-23.1	-2.9	-9
506	GAACTTGGGGAAACTGAACA SEQ.ID.NO:2017	2.8	-19.8	58.3	-22.1	-0.2	-2.5
543	AGGTTGGAATAATAGGATGA SEQ.ID.NO:2018	2.8	-18.7	57.8	-21.5	0	-1.3
547	ACCCAGGTTGGAATAATAGG SEQ.ID.NO:2019	2.8	-22.4	64.4	-24.3	-0.8	-4.3
556	GGGGTAGAAACCCAGGTTGG SEQ.ID.NO:2020	2.8	-26.3	73.1	-25	-4.1	-9.1
944	TACACTGAATTTCAGTTAAC SEQ.ID.NO:2021	2.8	-17.4	55.5	-17.7	-2.5	-11.3
1355	GAAGTTTCTTATTGAAAATC SEQ.ID.NO:2022	2.8	-15.4	51.1	-16.7	-1.4	-5.8
1448	TACTTTTATAAAAACTAAAC SEQ.ID.NO:2023	2.8	-11.3	42.2	-13.6	0	-7.8
1450	AATACTTTTATAAAAACTAA SEQ.ID.NO:2024	2.8	-11.1	41.8	-13.4	0	-7.6
1837	GGGTACAAGTGAAATAAAGG SEQ.ID.NO:2025	2.8	-17.4	54.1	-20.2	0	-5.2
8	GAGGTGAGGAGGAGGAGAGA SEQ.ID.NO:2026	2.9	-24.2	72.3	-27.1	0	0
417	ACACCAAATAAATTTTCAGA SEQ.ID.NO:2027	2.9	-16.7	52.4	-19.6	0	-4.7
554	GGTAGAAACCCAGGTTGGAA SEQ.ID.NO:2028	2.9	-23.8	67.2	-25.8	-0.8	-7
561	TGCTGGGGGTAGAAACCCAG SEQ.ID.NO:2029	2.9	-26.5	72.8	-25.3	-4.1	-10.8
1172	CACTGAATTCTTCTTTTAAA SEQ.ID.NO:2030	2.9	-17.1	54.5	-19.3	-0.4	-6.9
1447	ACTTTTATAAAAACTAAACA SEQ.ID.NO:2031	2.9	-12.3	44	-14.7	0	-7.8
1453	CCCAATACTTTTATAAAAAC SEQ.ID.NO:2032	2.9	-15.9	50.3	-18.3	0	-7.8
1457	GTTCCCCAATACTTTTATAA SEQ.ID.NO:2033	2.9	-21.5	62.8	-24.4	0	-3.7
1875	ACAACATAAATATTCATCAA	2.9	-14.7	48.7	-17.6	0	-4.6

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intra-molecular oligo	kcal/mol Inter-molecular oligo
	SEQ.ID.NO:2034						
17	GGAGACAATGAGGTGAGGAG SEQ.ID.NO:2035	3	-22	65.5	-25	0	-2.7
407	AATTTTCAGAAAAAGAAAAT SEQ.ID.NO:2036	3	-11	41.4	-11.5	-2.5	-8.1
945	TTACACTGAATTTCAGTTAA SEQ.ID.NO:2037	3	-17.3	55.3	-17.8	-2.5	-11.3
1185	AAATTTTCTTCTGCACTGAA SEQ.ID.NO:2038	3	-19.1	58.6	-22.1	0	-4.8
2	AGGAGGAGGAGAGAGTCTCG SEQ.ID.NO:2039	3.1	-24.3	72.4	-25	-2.4	-10
504	ACTTGGGGAAACTGAACATT SEQ.ID.NO:2040	3.1	-20	59.3	-22.6	-0.2	-2.5
1179	TCTTCTGCACTGAATTCTTC SEQ.ID.NO:2041	3.1	-22.1	67.5	-25.2	0	-6.9
1442	TATAAAAACTAAACATAGGT SEQ.ID.NO:2042	3.1	-13	45.3	-16.1	0	-3.2
1558	CTGAAGCTTCTCTACTGCCT SEQ.ID.NO:2043	3.1	-25.7	74.2	-27.4	0	-10.8
1702	TACTCTCCATGACATCAGCA SEQ.ID.NO:2044	3.1	-24.3	70.9	-27.4	0	-4.5
1873	AACATAAATATTCATCAAGA SEQ.ID.NO:2045	3.1	-14.4	48.3	-17.5	0	-4.6
1880	TAATTACAACATAAATATTC SEQ.ID.NO:2046	3.1	-12.4	44.4	-15.5	0	-4.6
1171	ACTGAATTCTTCTTTTAAAA SEQ.ID.NO:2047	3.2	-15.7	51.5	-18.2	-0.4	-6.9
1173	GCACTGAATTCTTCTTTTAA SEQ.ID.NO:2048	3.2	-19.6	60.5	-22.8	0.3	-6.2
403	TTCAGAAAAAGAAAATTCAT SEQ.ID.NO:2049	3.3	-12.7	44.6	-15.1	-0.7	-4.8
1827	GAAATAAAGGAAAGTTATAC SEQ.ID.NO:2050	3.3	-12.8	45	-16.1	0	-2.8
258	TGAGGAAATGTCCAGAAGAA SEQ.ID.NO:2051	3.4	-19.1	57.5	-20.4	-2.1	-4.9
292	CAAAAAAAACTCCAAAGTGT SEQ.ID.NO:2052	3.4	-15	48.3	-17.7	-0.5	-3
372	AAATGGGAATGTTCAATGAG SEQ.ID.NO:2053	3.5	-17.2	53.8	-20.7	0	-5.7
1188	AGAAAATTTTCTTCTGCACT SEQ.ID.NO:2054	3.5	-19.1	58.9	-20.9	-0.5	-11.6
1634	GGAGACAGGCAAAGTGTTGA SEQ.ID.NO:2055	3.5	-22.7	66.8	-25.3	-0.7	-4
7	AGGTGAGGAGGAGGAGAGAG SEQ.ID.NO:2056	3.6	-23.6	71.2	-27.2	0	0
500	GGGGAAACTGAACATTGCTG SEQ.ID.NO:2057	3.6	-21.5	62.2	-24.6	-0.2	-3.8
784	GAAACCTTTACACCCCTCAC SEQ.ID.NO:2058	3.6	-25.5	69.4	-29.1	0	-2
1514	CTGGAGACAGGATAACAATT SEQ.ID.NO:2059	3.6	-19.3	58.4	-21.1	-1.8	-5.9
256	AGGAAATGTCCAGAAGAAAT SEQ.ID.NO:2060	3.7	-17.8	54.6	-19.4	-2.1	-4.9
515	TCTGTGGTTGAACTTGGGGA SEQ.ID.NO:2061	3.7	-24.3	71.2	-28	0	-3.4

position	oligo	kcal/ mol total binding	kcal/ mol duplex forma- tion	deg C Tm of Duplex	kcal/ mol target struc- ture	kcal/ mol Intra- mole- cular oligo	kcal/ mol Inter- mole- cular oligo
775	ACACCCCTCACAGGTCAGTG SEQ.ID.NO:2062	3.8	-28.7	79.9	-31.4	-1	-5.4
401	CAGAAAAAGAAAATTCATCT SEQ.ID.NO:2063	3.9	-13.5	46.1	-16.5	-0.7	-4.8
260	CTTGAGGAAATGTCCAGAAG SEQ.ID.NO:2064	4	-20.2	60.3	-22.8	-1.3	-5.5
408	AAATTTTCAGAAAAAGAAAA SEQ.ID.NO:2065	4	-10.3	40.1	-12.7	-1.6	-8.1
409	TAAATTTTCAGAAAAAGAAA SEQ.ID.NO:2066	4	-10.7	40.9	-13.8	-0.8	-8.1
723	CAAACAACACACACAGCTCATC SEQ.ID.NO:2067	4	-20.4	60.2	-24.4	0	-4.4
1459	CAGTTCCCCAATACTTTTAT SEQ.ID.NO:2068	4	-23.2	66.7	-27.2	0	-2.9
13	ACAATGAGGTGAGGAGGAGG SEQ.ID.NO:2069	4.1	-22.6	66.8	-26.7	0	-3.1
295	CTTCAAAAAAAACTCCAAAG SEQ.ID.NO:2070	4.1	-14	46.5	-18.1	0	-2
462	ACTTCCAGGTTCTGTCCCAG SEQ.ID.NO:2071	4.1	-28.4	81.2	-32	-0.1	-3.7
402	TCAGAAAAAGAAAATTCATC SEQ.ID.NO:2072	4.2	-13	45.3	-16.3	-0.7	-4.8
940	CTGAATTTCAGTTAACAAGC SEQ.ID.NO:2073	4.2	-18.4	57.2	-21.5	-1	-8.4
1356	GGAAGTTTCTTATTGAAAAT SEQ.ID.NO:2074	4.2	-16.2	52.4	-19.4	-0.9	-6.6
1446	CTTTTATAAAAACTAAACAT SEQ.ID.NO:2075	4.2	-12.1	43.5	-15.8	0	-7.8
410	ATAAATTTTCAGAAAAAGAA SEQ.ID.NO:2076	4.3	-11.4	42.2	-15.1	-0.3	-7.6
1458	AGTTCCCCAATACTTTTATA SEQ.ID.NO:2077	4.3	-22.2	65	-26.5	0	-2.8
413	CAAATAAATTTTCAGAAAAA SEQ.ID.NO:2078	4.4	-10.8	41	-14.4	-0.6	-8.1
420	AAAACACCAAATAAATTTTC SEQ.ID.NO:2079	4.4	-13.3	45.4	-17.7	0	-4.7
622	GAGAGTCTCAGCTGGCATAC SEQ.ID.NO:2080	4.4	-25.1	75.3	-28.6	-0.3	-9.3
501	TGGGGAAACTGAACATTGCT SEQ.ID.NO:2081	4.5	-21.5	62.2	-25.5	-0.2	-3.8
2039	TTCCCTAGTTCAACAGATAG SEQ.ID.NO:2082	4.5	-22	65.7	-26.5	0	-3.6
725	CACAAACAACACACACAGCTCA SEQ.ID.NO:2083	4.6	-20.9	60.6	-25.5	0	-4.4
942	CACTGAATTTCAGTTAACAA SEQ.ID.NO:2084	4.6	-17.5	54.9	-19.6	-2.5	-11.3
1456	TTCCCCAATACTTTTATAAA SEQ.ID.NO:2085	4.6	-19.6	58	-24.2	0	-5.7
296	TCTTCAAAAAAAACTCCAAA SEQ.ID.NO:2086	4.8	-14.4	47.3	-19.2	0	-1
423	GTTAAAACACCAAATAAATT SEQ.ID.NO:2087	4.8	-13.7	46.1	-18.5	0	-4.1
763	GGTCAGTGCATTATAGTGGT SEQ.ID.NO:2088	4.8	-24.3	74.1	-29.1	0	-5.4
9	TGAGGTGAGGAGGAGGAGAG	4.9	-23.6	70.7	-28.5	0	0

position	oligo	kcal/ mol total binding	kcal/ mol duplex formation	deg C Tm of Duplex	kcal/ mol target structure	kcal/ mol Intra-molecular oligo	kcal/ mol Inter-molecular oligo
	SEQ.ID.NO:2089						
560	GCTGGGGGTAGAAACCCAGG SEQ.ID.NO:2090	4.9	-27.7	75.4	-28.3	-4.3	-10.9
1460	TCAGTTCCCCAATACTTTTA SEQ.ID.NO:2091	4.9	-23.6	68.3	-28.5	0	-2.9
244	GAAGAAATCCAGGAAACTAA SEQ.ID.NO:2092	5	-16.7	51.9	-21.1	-0.3	-5.7
418	AACACCAAATAAATTTTCAG SEQ.ID.NO:2093	5.1	-15.4	49.6	-20.5	0	-4.7
528	GATGACGAGGAAATCTGTGG SEQ.ID.NO:2094	5.1	-20.9	61.4	-26	0	-3.3
1187	GAAAATTTTCTTCTGCACTG SEQ.ID.NO:2095	5.1	-19.1	58.6	-23.1	0	-10.1
765	CAGGTCAGTGCATTATAGTG SEQ.ID.NO:2096	5.2	-22.6	69.1	-27.8	0	-5.4
774	CACCCCTCACAGGTCAGTGC SEQ.ID.NO:2097	5.2	-30.3	83.7	-34.8	-0.5	-5.9
1443	TTATAAAAACTAAACATAGG SEQ.ID.NO:2098	5.2	-11.9	43.1	-17.1	0	-3.5
3	GAGGAGGAGGAGAGAGTCTC SEQ.ID.NO:2099	5.3	-24.1	74	-28	-1.3	-8.7
724	ACAAACAACACACAGCTCAT SEQ.ID.NO:2100	5.4	-20.2	59.5	-25.6	0	-4.4
529	GGATGACGAGGAAATCTGTG SEQ.ID.NO:2101	5.5	-20.9	61.4	-25.9	-0.1	-3.7
762	GTCAGTGCATTATAGTGGTA SEQ.ID.NO:2102	5.6	-22.8	70.5	-28.4	0	-5
422	TTAAAACACCAAATAAATTT SEQ.ID.NO:2103	5.7	-12.6	44.1	-18.3	0	-4.5
411	AATAAATTTTCAGAAAAAGA SEQ.ID.NO:2104	5.8	-11.4	42.2	-16.3	-0.8	-8.1
764	AGGTCAGTGCATTATAGTGG SEQ.ID.NO:2105	5.8	-23.1	70.7	-28.9	0	-5.4
243	AAGAAATCCAGGAAACTAAG SEQ.ID.NO:2106	5.9	-16.1	50.9	-21.4	-0.3	-5.7
1101	ATAAAATGTAGAAGAGTCTG SEQ.ID.NO:2107	5.9	-15.5	51.1	-20.9	-0.2	-5.8
5	GTGAGGAGGAGGAGAGAGTC SEQ.ID.NO:2108	6	-24	73.5	-30	0	-3.5
1874	CAACATAAATATTCATCAAG SEQ.ID.NO:2109	6	-14.5	48.3	-20.5	0	-4.6
425	CTGTTAAAACACCAAATAAA SEQ.ID.NO:2110	6.2	-14.5	47.5	-20.7	0	-5.5
941	ACTGAATTTCAGTTAACAAG SEQ.ID.NO:2111	6.3	-16.8	53.8	-20.8	-2.3	-11
512	GTGGTTGAACTTGGGGAAAC SEQ.ID.NO:2112	6.4	-21.8	64	-28.2	0	-3.4
10	ATGAGGTGAGGAGGAGGAGA SEQ.ID.NO:2113	6.5	-23.6	70.4	-30.1	0	-0.3
424	TGTTAAAACACCAAATAAAT SEQ.ID.NO:2114	6.6	-13.6	45.8	-20.2	0	-5.4
1519	TCTATCTGGAGACAGGATAA SEQ.ID.NO:2115	6.6	-20.4	62.4	-25.2	-1.8	-9.5
421	TAAAACACCAAATAAATTTT SEQ.ID.NO:2116	6.7	-12.6	44.1	-19.3	0	-4.7

position	oligo	kcal/mol total binding	kcal/mol duplex formation	deg C Tm of Duplex	kcal/mol target structure	kcal/mol Intra-molecular oligo	kcal/mol Inter-molecular oligo
419	AAACACCAAATAAATTTTCA SEQ.ID.NO:2117	6.8	-14.7	48	-21.5	0	-4.7
507	TGAACTTGGGGAAACTGAAC SEQ.ID.NO:2118	6.9	-19.1	57.1	-25.5	-0.2	-1.8
513	TGTGGTTGAACTTGGGGAAA SEQ.ID.NO:2119	7	-21.6	63.3	-28.6	0	-3.4
510	GGTTGAACTTGGGGAAACTG SEQ.ID.NO:2120	7.1	-21.5	62.8	-28.1	-0.2	-3.6
412	AAATAAATTTTCAGAAAAAG SEQ.ID.NO:2121	7.3	-10.1	39.8	-16.5	-0.8	-8.1
294	TTCAAAAAAAACTCCAAAGT SEQ.ID.NO:2122	7.5	-14.3	47.2	-21.2	-0.3	-2.9
511	TGGTTGAACTTGGGGAAACT SEQ.ID.NO:2123	7.5	-21.5	62.8	-28.5	-0.2	-3.6
758	GTGCATTATAGTGGTATCCA SEQ.ID.NO:2124	7.6	-23.6	70.6	-30.5	-0.4	-6.2
1417	ATATTCATCAGAGATACCAC SEQ.ID.NO:2125	7.6	-20	61.3	-27.6	0	-3.5
1416	TATTCATCAGAGATACCACT SEQ.ID.NO:2126	7.7	-20.9	63.3	-28.6	0	-3.5
11	AATGAGGTGAGGAGGAGGAG SEQ.ID.NO:2127	7.8	-22.3	66.6	-30.1	0	-1.2
508	TTGAACTTGGGGAAACTGAA SEQ.ID.NO:2128	7.9	-19	57	-26.4	-0.2	-1.8
757	TGCATTATAGTGGTATCCAG SEQ.ID.NO:2129	7.9	-22.4	67.4	-29.5	-0.6	-5.8
1415	ATTCATCAGAGATACCACTA SEQ.ID.NO:2130	8	-20.9	63.3	-28.9	0	-3.5
12	CAATGAGGTGAGGAGGAGGA SEQ.ID.NO:2131	8.1	-23	67.6	-31.1	0	-1.6
761	TCAGTGCATTATAGTGGTAT SEQ.ID.NO:2132	8.5	-21.6	66.9	-30.1	0	-6.3
509	GTTGAACTTGGGGAAACTGA SEQ.ID.NO:2133	8.6	-20.9	61.6	-29	-0.2	-3.2
1455	TCCCCAATACTTTTATAAAA SEQ.ID.NO:2134	8.7	-18.8	56	-27	0	-7.5
1454	CCCCAATACTTTTATAAAAA SEQ.ID.NO:2135	8.8	-17.7	53.3	-26	0	-7.8
293	TCAAAAAAAACTCCAAAGTG SEQ.ID.NO:2136	8.9	-14.2	46.9	-22.4	-0.5	-3
759	AGTGCATTATAGTGGTATCC SEQ.ID.NO:2137	9.6	-22.9	69.6	-32.5	0	-6.3
760	CAGTGCATTATAGTGGTATC SEQ.ID.NO:2138	14.3	-21.6	66.9	-35.9	0	-6.3

Example 15

Western blot analysis of FXR protein levels

[00188] Western blot analysis (immunoblot analysis) is carried out using standard methods. Cells are harvested 16-20 h after oligonucleotide treatment,

washed once with PBS, suspended in Laemmli buffer (100 ul/well), boiled for 5 minutes and loaded on a 16% SDS-PAGE gel. Gels are run for 1.5 hours at 150 V, and transferred to membrane for western blotting. Appropriate primary antibody directed to FXR is used, with a radiolabeled or fluorescently labeled secondary antibody directed against the primary antibody species. Bands are visualized using a PHOSPHORIMAGER™ (Molecular Dynamics, Sunnyvale CA).